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## **TITLE OF THE INVENTION**

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Crystalline TNF- $\alpha$ -Converting Enzyme and Uses Thereof

## **INFORMATION ON RELATED APPLICATIONS**

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This application is a continuation of U.S. Serial No. 09/611,722 filed July 6, 2000, which is a divisional of U.S. Serial No. 09/244,984 filed on February 4, 1999, both of which are hereby incorporated herein by reference. U.S. Serial No. 09/244,984 claims the priority benefit of U.S. Provisional Application No. 60/117,476 filed on January 27, 1999, U.S. Provisional Application No. 60/135,499 filed on March 30, 1998, and U.S. Provisional Application No. 60/073,709 filed on February 4, 1998.

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## **BACKGROUND OF THE INVENTION**

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The cytokine tumor necrosis factor- $\alpha$  (TNF $\alpha$ ) plays a role in the induction of inflammatory reactions and is known to be cytotoxic towards tumor cells. TNF $\alpha$ , however, also may cause severe damage to the human body when produced in excess by eventually leading to multiple organ failure and death. See Bemelmans *et al.*, "Tumor Necrosis Factor: Function, Release and Clearance," *Crit. Rev. Immun.* 16: 1-11 (1996).

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Tumor necrosis factor- $\alpha$  is produced by activated cells, such as mononuclear phagocytes, T-Cells, B-Cells, mast cells and NK cells. TNF $\alpha$  exists in two forms: a type II membrane protein having a relative molecular mass of 26 kD and a soluble 17 kD form generated from the membrane form by proteolytic cleavage. The TNF $\alpha$  membrane protein is synthesized as a 223 amino acid membrane-anchored precursor.

The soluble TNF $\alpha$  is released from the membrane-bound precursor by a membrane-anchored proteinase. This proteinase was recently identified as a multidomain metalloproteinase called TNF $\alpha$ -converting enzyme (TACE). See, Black *et al.*, "A metalloproteinase disintegrin that releases tumor-necrosis factor- $\alpha$  from cells," Nature 385: 729-733 (1997), Moss *et al.*, "Cloning of a disintegrin metalloproteinase that processes precursor tumor-necrosis factor- $\alpha$ ," Nature 385: 733-736 (1997). TACE has recently been identified as a zinc endopeptidase consisting of an extracellular region comprising an N-terminal signal peptide, a pro-domain, a 263 residue catalytic domain (TCD) that is preceded by a furin cleavage site (residues 211-214), a disintegrin domain, an EFF-like domain, and a crambin-like domain, an apparent transmembrane helix and the intracellular C-terminal tail. Tumor necrosis factor- $\alpha$  converting enzyme (TACE), including a polynucleotide sequence, is described in detail in the published PCT application No. WO 96/41624, herein incorporated in the entirety by reference.

As noted above, the over-production or unregulated production of TNF- $\alpha$  presents serious physiological dangers. It has been implicated in various deleterious physiological diseases such as rheumatoid arthritis, cachexia and endotoxic shock. It also may eventually lead to organ failure and death. Thus, a way to control or block release of TNF $\alpha$  into the circulation is needed. Because of TACE's role in the conversion of TNF $\alpha$ , inhibition, modulation, or regulation of TACE would affect the release of TNF $\alpha$  into circulation. Inhibitors of metalloproteinases and structure based design thereof are described in Zask *et al.*, "Inhibition of Matrix Metalloproteinases: Structure Based Design" *Current Pharmaceutical Design*, 2:624-661 (1996). Thus, compounds that associate with TACE, such as inhibitors, receptors or modulators will be useful to protect patients from adverse effects associated with the over-production or unregulated production of tumor necrosis factor- $\alpha$ .

## SUMMARY OF THE INVENTION

According to one aspect of the invention, there is provided a composition comprising a polypeptide in crystalline form, wherein the polypeptide is a TNF- $\alpha$ -

converting enzyme polypeptide. In one embodiment, the TNF- $\alpha$ -converting enzyme polypeptide comprises the TNF- $\alpha$ -converting enzyme catalytic domain. In another embodiment, the TNF- $\alpha$ -converting enzyme polypeptide is the expression product of a polynucleotide encoding the pro and catalytic domains of TNF- $\alpha$ -converting enzyme. In a further embodiment, the TNF- $\alpha$ -converting enzyme polypeptide is the expression product of a polynucleotide encoding the amino acid residues 1-477 of TNF- $\alpha$ -converting enzyme. In yet another embodiment, the polynucleotide is substituted such that amino acid residue Ser266 is changed to Ala and amino acid residue Asn542 is changed to Gln, and wherein a second polynucleotide encoding the sequence Gly-Ser-(His)<sub>6</sub> (SEQ ID NO: 2) is fused to the C-terminus.

According to another aspect of the invention, the compositions above further comprising a binding partner suitable for co-crystallization with the TNF- $\alpha$ -converting enzyme polypeptide. In one embodiment, the binding partner is a hydroxamate-based binding partner. In another embodiment, the binding partner is N-{D,L-2-(hydroxyaminocarbonyl)methyl-4-methylpentanoyl}-L-3-amino-2-dimethylbutanoyl-L-alanine,2-(amino)ethyl amide.

According to further embodiments, the compositions above have a crystal structure diffracting to 2.0 Å, are monoclinic, have a unit cell comprising four crystallographically independent TNF- $\alpha$ -converting enzyme catalytic domain (TCD) molecules, have the TCD molecules are in an asymmetric unit, and/or have monoclinic space group P2<sub>1</sub> and the cell has the constants a=61.38 Å, b=126.27 Å, c=81.27 Å, and  $\beta$ =107.41°.

In still another embodiment of the invention, the polypeptides above are characterized by the structure coordinates according to Table 1, or a substantial part thereof.

According to a further aspect of the invention, there is provided a method for crystallizing a TNF- $\alpha$ -converting enzyme polypeptide, comprising (A) mixing a solution comprising a TACE polypeptide and a binding partner with a crystallization buffer; and (B) crystallizing the mixture of step (A) by drop vapor diffusion to form a

crystalline precipitate. In one embodiment, the method further comprises (C) transferring seeds from the crystalline precipitate formed by the drop vapor diffusion and a crystallization promotor into a mixture of a concentrated solution comprising a TACE polypeptide and binding partner substrate, and a crystallization buffer; and (D) crystallizing the mixture of step (C) by drop vapor diffusion to form a crystal. In another embodiment, the crystallization buffer is 0.1M Na Citrate pH 5.4, 20%w/v PEG 4000, and 20% v/v Isopropanol. In still another embodiment, the binding partner is N-{D,L-2-(hydroxyaminocarbonyl)methyl-4-methylpentanoyl}-L-3-amino-2-dimethylbutanoyl-L-alanine, 2-(amino)ethyl amide. In yet another embodiment, crystallization is at a temperature ranging from 4 to 20 degrees Celsius. In another embodiment, the solution comprising the TACE polypeptide and the inhibitor is at a concentration of about 5 mg/mL to about 12 mg/mL in a buffer. In a further embodiment, the solution comprising a TACE polypeptide and the binding partner is mixed with the crystallization buffer in a 1:1 ratio.

According to still another aspect of the invention, there is provided a tumor necrosis factor- $\alpha$  (TNF- $\alpha$ )-converting enzyme crystal made by co-crystallizing a TNF- $\alpha$ -converting enzyme polypeptide with a co-crystallization substrate.

According to yet another aspect of the invention, there is provided a computer-readable medium having recorded thereon x-ray crystallographic coordinate data for the catalytic domain of TNF- $\alpha$  converting enzyme, or a portion thereof. In one embodiment, the computer-readable medium has recorded thereon the x-ray crystallographic coordinate data set forth in Table 1, or a portion thereof. In another embodiment, the medium is selected from the group consisting of a floppy disc, a hard disc, computer tape, RAM, ROM, CD, DVD, a magnetic disk, and an optical disk. In still another embodiment, the computer-readable medium has recorded thereon machine-readable data, wherein the computer-readable medium, when used in conjunction with a machine programmed with instructions for using the data, is capable of generating image signals for depicting a graphical, three-dimensional representation of a TNF- $\alpha$  converting enzyme polypeptide, or portion thereof.

According to a further aspect of the invention, there is provided a system for studying a TNF- $\alpha$  converting enzyme polypeptide, said system comprising (a) a memory capable of storing information representing at least a portion of a TNF- $\alpha$  converting enzyme polypeptide, wherein said memory comprises at least one first-type storage region, including a set of spatial coordinates specifying a location in a three dimensional space, and at least one second-type storage region comprising information representing a characteristic of one of a plurality of amino acids, said second-type storage regions being logically associated with said first-type storage regions in said memory to represent a geometric arrangement of at least one characteristic of said at least a portion of said TNF- $\alpha$  converting enzyme peptide in said three dimensional space; (b) a processor coupled to said memory to access said first-type storage regions and said second-type storage regions, wherein the processor generates image signals for depicting a visual image representing three dimensional image of said at least one characteristic of said at least a portion of said TNF- $\alpha$  converting enzyme polypeptide in said three dimensional space based on data from said memory; and (c) a display coupled to said processor to receive said image signals, wherein the display depicts a visual three dimensional image of said at least one characteristic of said at least a portion of said TNF- $\alpha$  converting enzyme polypeptide in said three dimensional space based on said image signals. In one embodiment of the invention, the image signals include signals for depicting a visual three dimensional image of a ribbon structure of said at least a portion of said TNF- $\alpha$  converting enzyme polypeptide in said three dimensional space. In another embodiment of the invention, the image signals include signals for depicting a visual image of a solid model representation of said at least a portion of said TNF- $\alpha$  converting enzyme polypeptide in said three dimensional space. In still another embodiment of the invention, the image signals include signals for depicting a visual three dimensional image of electrostatic surface potential of said at least a portion of said TNF- $\alpha$  converting enzyme polypeptide in said three dimensional space. In yet another embodiment of the invention, the image signals include signals for depicting a

visual three dimensional stereo image of said at least a portion of said TNF- $\alpha$  converting enzyme polypeptide in said three dimensional space. In a further embodiment of the invention, the system further comprises a storage device capable of storing data representing a geometric arrangement of a characteristic of a composition other than said TNF- $\alpha$  converting enzyme polypeptide; and an operator interface for receiving instructions from a operator; and wherein said processor is coupled to said storage device and to said operator interface and generates additional image signals for depicting said geometric arrangement of said characteristic of said composition relative to said visual three dimensional image of said at least one characteristic of said at least a portion of said TNF- $\alpha$  converting enzyme polypeptide on said display based on instructions from the operator interface. In one embodiment, the storage device is part of said memory. In another embodiment, the system comprises a plurality of first-type and second-type storage regions.

According to another aspect of the invention, there is provided a video memory capable of storing information for generating a visual display of at least a portion of a TNF- $\alpha$  converting enzyme polypeptide, said video memory comprising (a) at least one first-type storage region, each of said first-type storage regions including a set of spatial coordinates specifying a location in a three dimensional space; and (b) at least one second-type storage region, each of said second-type storage regions containing information for visually depicting a characteristic of one of a plurality of amino acids; wherein said second-type storage regions are logically associated with said first-type storage regions in said video memory to represent a geometric arrangement of at least one characteristic of said at least a portion of said TNF- $\alpha$  converting enzyme polypeptide in said three dimensional space. In one embodiment, the second-type storage regions are logically associated with said first-type storage regions in said video memory to represent a geometric arrangement of at least one characteristic of a catalytic domain portion of said TNF- $\alpha$  converting enzyme polypeptide in said three dimensional space. In another embodiment, the first-type storage regions and said second-type storage regions are regions of a

semiconductor memory. In yet another embodiment, the first-type storage regions and said second-type storage regions are regions of an optical disk. In still another embodiment, the first-type storage regions and said second-type storage regions are regions of a magnetic memory. In a further embodiment, the video memory comprises a plurality of first-type and second-type storage regions.

In a still further aspect of the invention, there is provided a method of identifying a compound that associates with TNF- $\alpha$ -converting enzyme, comprising (A) designing an associating compound for said polypeptide that forms a bond with the TNF- $\alpha$ -converting enzyme catalytic domain based on x-ray diffraction coordinates of a TNF- $\alpha$ -converting enzyme polypeptide crystal; (B) synthesizing said compound; and (C) determining the associate capability of said compound with said TNF- $\alpha$ -converting enzyme. In one embodiment, the associating compound is an inhibitor, mediator, or other compound that regulates TNF- $\alpha$ -converting enzyme activity. In another embodiment, the associating compound is a competitive inhibitor, un-competitive inhibitor, or non-competitive inhibitor. In still another embodiment, the coordinates are the coordinates of Table 1, or a substantial part thereof. In a further embodiment, the TNF- $\alpha$ -converting enzyme polypeptide crystal comprises the TNF- $\alpha$ -converting enzyme catalytic domain. In still another embodiment, the TNF- $\alpha$ -converting enzyme polypeptide is the expression product of a polynucleotide encoding the pro and catalytic domains of TNF- $\alpha$ -converting enzyme. In yet another embodiment, the TNF- $\alpha$ -converting enzyme polypeptide is the expression product of a polynucleotide encoding the amino acid residues 1-477 of TNF- $\alpha$ -converting enzyme. In another embodiment, the polynucleotide is substituted such that amino acid residue Ser266 is changed to Ala and amino acid residue Asn542 is changed to Gln, and wherein a second polynucleotide encoding the sequence Gly-Ser-(His)<sub>6</sub> (SEQ ID NO: 2) is fused to the C-terminus. In a further embodiment, the TNF- $\alpha$ -converting enzyme polypeptide crystal is co-crystallized with a binding partner. In still another embodiment, the binding partner is a hydroxamate-based binding partner or N-{D,L-2-(hydroxyaminocarbonyl) methyl-4-methylpentanoyl}-L-3-amino-2-

dimethylbutanoyl-L-alanine,2-(amino)ethyl amide. In yet other embodiments, the TNF- $\alpha$ -converting enzyme polypeptide crystal has a crystal structure diffracting to 2.0 Å, is monoclinic, has a unit cell comprising four crystallographically independent TNF- $\alpha$ -converting enzyme catalytic domain (TCD) molecules, has the TCD molecules are in an asymmetric unit, and/or is of monoclinic space group  $P2_1$  and the cell has the constants  $a=61.38$  Å,  $b=126.27$  Å,  $c=81.27$  Å, and  $\beta=107.41^\circ$ . In still another embodiment, the invention the associating compound is designed to associate with the S1' region of TNF- $\alpha$ -converting enzyme. In yet another embodiment, the associating compound is designed to associate with the S1'S3' pocket of TNF- $\alpha$ -converting enzyme. In still other embodiments of the invention, the associating compound is designed to (i) incorporate a moiety that chelates zinc, (ii) form a hydrogen bond with Leu348 or Gly349 of TNF- $\alpha$ -converting enzyme, (iii) introduce a non-polar group which occupies the S1' pocket of TNF- $\alpha$ -converting enzyme, (iv) introduce a group which lies within the channel joining S1' - S3' pockets of TNF- $\alpha$ -converting enzyme and which makes appropriate van der Waal contact with the channel, and/or (v) form a hydrogen bond with Leu348 or Gly349 on the backbone amide groups of TNF- $\alpha$ -converting enzyme.

These and other aspects of the invention will become apparent to the skilled artisan in view of the teachings contained herein.

## BRIEF DESCRIPTION OF THE FIGURES

**Fig. 1:** Figure 1 is a ribbon diagram of the TACE catalytic domain (TCD). The chain starts on the lower left back side, runs through the structural elements sI, hAI, hA, sII, hB, hB2, sIII, IV, IVa, sIVb, sV, hC, Met-turn and hD, and ends in the upper left back. The three disulfides are shown as connections, with the sulphurs given as small spheres. The catalytic zinc (central sphere) is liganded by the three imidazoles of His405, His409 and His415, and by the hydroxyl and the carbonyl oxygen atoms of the inhibitor hydroxamic acid group. The inhibitor mimicking interaction of primed-site residues of a peptide substrate is shown in full. Figure 1 was



made using SETOR. See Evans, S. "SETOR: Hardware Lighted Three-Dimensional Solid Model Representations of Macromolecules" *J. Mol. Graph.* 11:134-138 (1993).

**Figs. 2a and 2b:** Figures 2a and 2b are solid surface representations of the catalytic domains of TACE (TCD) (Figure 2a) and MMP-3 (Figure 2b). The electrostatic surface potential is contoured from -15 (intense red) to 15 (intense blue)  $k_B T/e$ . Both active-site clefts run from left to right, with the catalytic zinc atoms (spheres) in the centers. In TACE, the bound inhibitor is shown in full structure, binding with its isobutyl (P1') and its Ala (P3') sidechains into the deep S1' and the novel S3' pockets. The orientation is similar to Fig. 1. Figures 2a and 2b were made using GRASP. Nicolls, A., Bharadwaj, R. and Houig, B., "Grasp - Graphical representation and analysis of surface properties," *Biophys.* 64, A166 (1993).

**Fig. 3:** Figure 3 aligns the catalytic domain sequences of adamalysin II (ADAM\_CROAD) (SEQ ID NO: 4), TACE (SEQ ID NO: 5) and human ADAM 10 (hADAM10) (SEQ ID NO: 6), according to their topological equivalence and sequence similarity, respectively. The residue numbers are due to the generic TACE numbering. Arrows and braces represent  $\beta$ -strands and  $\alpha$ -helices in TACE.

**Fig. 4:** Figure 4 is a stereo section of the final 2.0 Å electron density around the catalytic zinc (large, central sphere) superimposed with the final TACE model. Visible are the three zinc liganding imidazole rings of His405 (top), His409 (left) and His415 (bottom), the "catalytic" Glu406, and the hydroxamic acid moiety of the inhibitor. The orientation is similar to Fig. 1. Figure 4 was made using TURBO-FRODO. See Roussel, A. & Cambilleau, C., "Turbo-Frodo in Silicon Graphics Geometry," *Partners Directory*, Silicon Graphics, Mountain View, CA (1989).

**Fig. 5:** Figure 5 is a superposition of the ribbon plots of the catalytic domain of TACE (light) and adamalysin (dark). Also shown is the catalytic zinc of TACE (sphere) and the three (TACE) and two (adamalysin) disulfide bridges. The orientation is similar to Fig. 1. Figure 5 was made using GRASP.

**Fig. 6:** Figure 6 illustrates a system for studying a TNF- $\alpha$  converting enzyme, including a video memory storing information for generating a visual display of at least a portion of a TNF- $\alpha$  converting enzyme.

## DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to a highly purified tumor necrosis factor- $\alpha$  converting enzyme (TACE) polypeptide, a method of producing and purifying a TACE polypeptide, a method of crystallizing a TACE polypeptide, and a TACE polypeptide crystal. The invention further relates to a X-ray diffraction method using a TACE polypeptide crystal, and to a method of obtaining the X-ray crystallographic structural coordinates of a TACE polypeptide as well as the structural coordinates themselves. Still further, the present invention relates using the structural coordinates of a TACE polypeptide to elucidate the three-dimensional structure of a TACE polypeptide and designing and developing compounds that associate with TACE. Knowledge of the three-dimensional structure and structure coordinates provided according to the invention permit the skilled person to make compounds that will interact with TACE. Such interacting compounds can be made by a variety of techniques and design criteria, including those disclosed in *Protein Engineering* (Oxender and Fox, eds.) (Alan R. Liss, Inc. 1987).

As used herein, TACE refers to a group of polypeptides that are capable of converting the 26 kD cell membrane-bound form of TNF $\alpha$  into the soluble 17 kD form that comprises the C-terminal 156 residues of the TNF $\alpha$  protein. TACE encompasses proteins having the amino acid sequence described in PCT application No. WO 96/41624, herein incorporated in its entirety by reference, as well as any of those proteins having homology, preferably no less than 50%, more preferably at least 80% homology, still more preferably 90% homology to such sequence, at the amino acid level. Additionally, TACE further refers to the expression products of nucleotide sequences disclosed in PCT application No. WO 96/41624. TACE further encompasses the membrane-bound protein and soluble or truncated proteins comprising the extracellular portion of the protein and which retain biological activity and are capable of being secreted. Examples of such proteins are described in PCT application No. WO 96/41624.

The TACE amino acid sequence, or any part or residue thereof, can be found in Black *et al.*, "A Metalloproteinase disintegrin that releases tumour-necrosis factor- $\alpha$

from cells,” *Nature* 385: 729-733 (Feb. 1997), herein incorporated in the entirety by reference. Variations in the amino acid sequence of TACE are within the present invention as well. All references to the TACE amino acid sequence contained herein refer to the sequence in Black *et al.*, supra (SEQ ID NO: 7).

5 As used herein, the TACE catalytic domain (TCD) refers to the portion of a TACE polypeptide between residues 215 and 477 and including the preceding furin cleavage site (residues 211-214), or any part thereof that is capable of cleaving the peptide PLAQAVRSSS (SEQ ID NO: 1).

#### 10 Expression, Isolation and Purification of TACE Polypeptides

Tumor necrosis factor- $\alpha$  converting enzyme (TACE) is described in the published PCT application No. WO 96/41624. The application describes isolated nucleic acids encoding TACE or portions of TACE, expression vectors comprising a cDNA encoding TACE or portions thereof, and host cells transformed or transfected  
15 with the expression vectors comprising a cDNA encoding TACE or portions of TACE. The application further describes processes for producing TACE and portions thereof, for example by culturing transfected cells engineered to express TACE, followed by purification of the recombinantly produced TACE or portion thereof. Methods of isolating, expressing, and purifying a TACE polypeptide are described in  
20 detail in published PCT application No. WO 96/41624. The entirety of PCT 96/41624 is incorporated herein by reference.

According to the invention, cDNA encoding the signal peptide, pro and catalytic domains of TACE, *i.e.*, amino acid residues 1-477 (SEQ ID NO: 8) is inserted into a suitable expression vector and expressed in a suitable cell line. The  
25 cDNA also may include other regions that facilitate expression or achieve other objects that otherwise that do not depart from the essence of the invention, such as flanking regions.

The cDNAs encoding the TACE polypeptide, or functional portions thereof, such as the TCD, may be altered by addition, substitution, deletion, or insertion. Such  
30 alterations may be made, for example, to prevent glycosylation, prevent formation of

incorrect or undesired disulfide bridges, and/or enhance expression. Examples of such alterations are described in WO 96/41624 and can be carried out by the methods described therein and other conventional methods. TACE may also be conjugated. Such conjugates may comprise peptides added to facilitate purification and/or identification. Such peptides include, for example, poly-His peptides. Conjugation is described in U.S. Patent No. 5,011,912 and Hopp *et al.*, *Bio/Technology* 6:1204 (1988).

In one embodiment of the invention, the cDNA encodes a TNF- $\alpha$  converting enzyme polypeptide comprising the signal peptide, pro and catalytic domains of TACE (TCD), residues 1-477, with Ser266 changed to Ala and Asn452 changed to Gln. These substitutions are useful in preventing N-linked glycosylation. Additionally, the sequence Gly-Ser(His)<sub>6</sub> (SEQ ID NO: 2) may be added to the C-terminus. The addition of the sequence Gly-Ser(His)<sub>6</sub> (SEQ ID NO: 2) facilitates purification of the polypeptide using metal-chelate affinity resins, such as Ni-NTA resins.

Recombinant expression vectors containing the nucleotide sequence encoding TACE, or a portion thereof, may be prepared using well known methods. Suitable host cells for expression of TACE polypeptides include prokaryotic, yeast, and higher eukaryotic cells. Vectors and host cells suitable for use in the present invention are described in WO 96/41624. Further examples of suitable expression systems that can be employed to express recombinant TACE according to the present invention include mammalian or insect host cell culture expression systems, including baculovirus systems in insect cells (See Luckow and Summers, *Bio/Technology* 6:47 (1988)) and mammalian cell lines such as COS-7 cells (Gluzman *et al.*, *Cell* 23:175 (1981)). Additional examples are known in the art and include those described in WO 96/41624. In one embodiment of the invention, the TACE polypeptide is expressed in CHO cells. In this embodiment, the cells secrete a mixture of TACE polypeptide beginning with Val212 and Arg215.

In one embodiment, stable expressing cells may be selected by culturing the cells in a drug that kills those cells that do not incorporate the vector. Examples of

suitable selection methods are described in, for example, Kaufman, R.J., "Selection and coamplification of heterologous genes in mammalian cells," *Methods in Enzymology*, 185:537-566 (1990).

Purification of the expressed TACE polypeptide may be carried out by any suitable means, such as those described in WO 96/41624. According to one aspect of the invention, it is preferable to obtain a TACE polypeptide that is suitable for crystallization. In obtaining a TACE polypeptide suitable for crystallization, it is important that the process for purifying the TACE polypeptide is sufficient to yield a polypeptide pure enough to properly crystallize.

A preferred method of purification starts with a suitable amount of medium from the culture of TACE-secreting cells. This medium is generally a supernate of the culture. The medium contains the TACE polypeptide to be purified. Preferably, the TACE polypeptide is recombinantly produced using DNA coding for the TACE polypeptide with the sequence altered to encode a conjugate or conjugates that facilitate purification. For example, the sequence encoding Gly-Ser-(His)<sub>6</sub> (SEQ ID NO: 2) may be added to the C-terminus to facilitate purification using metal-chelate resins.

The medium is concentrated, for example, by diafiltration. Suitable diafiltration units include a Millipore 10K cut-off, 1 ft<sup>2</sup> TFF diafiltration unit. A suitable buffer solution is then added to the concentrated medium. Any suitable buffer may be used. One such suitable buffer contains 20 mM Tris (pH 7.5) and 300 mM NaCl.

The sample is reconcentrated and diluted numerous times. For example, the sample may be reconcentrated and diluted a second time with the buffer, reconcentrated again, diluted a third time with the buffer, and reconcentrated a final time. The sample retained in the diafiltration unit is recovered by a suitable method, such as by a back-flush method. The recovered material may then be filtered through a suitable membrane. Suitable membranes include, for example, 0.45 or 0.22 micron pore-size membranes. Azide is then added. The filtered sample may then be stored overnight at a low temperature, such as about 2-9 °C.

After overnight storage, imidazole from a stock solution in water and  $\text{ZnCl}_2$  from a stock solution in water are added to the filtered sample. The sample then is pumped over a suitable column. One suitable column, particularly when the TACE polypeptide is conjugated with the sequence Gly-Ser-(His)<sub>6</sub> (SEQ ID NO: 2) is a metal-chelate resin, such as a Ni-NTA resin.

The column is washed with a buffer, such as a buffer of 20 mM Tris pH 7.5, 300 mM NaCl, 5 mM imidazole, and 5 uM  $\text{ZnCl}_2$ . The TACE polypeptide is then eluted with an increasing gradient of imidazole. Fractions are collected in tubes containing glycerol in water Tris pH 8. Preferably, the glycerol solution is prepared the day of the column run.

An aliquot from each fraction is spotted on a membrane which is stained with amido black to determine which fractions contain a significant amount of protein. Alternatively, a small amount, for example 5  $\mu\text{l}$ , from each fraction may be used for gel analysis using Coomassie staining. The fractions with a significant amount of protein are pooled, and the pool is then concentrated with, for example, a diafiltration unit.

In some cases, aggregation of polypeptide may occur. In order to eliminate aggregates and further facilitate purification, an inhibitor of TACE, such as a hydroxamate-based inhibitor, may be added to the concentrated sample from a stock solution in water, and octylglucoside (commercially available from Boehringer Mannheim) is added from a stock solution in water. The sample is then incubated at room temperature for 15-24 hours.

Following incubation, the sample is applied to a size exclusion column. The column is first equilibrated with a suitable buffer, such as a buffer of 10 mM Tris pH 7.5, 100 mM NaCl, 10% glycerol. Suitable size exclusion columns include, for example, LKB 2135-365, packed with TSK-G3000 SWG or the like such as Superdex-200. The buffer is then pumped through the column. The highly purified TACE polypeptide can be detected by absorption at 280 nm.

A gel analysis of all fractions with significant protein is carried out to determine which fractions should be pooled. The size exclusion chromatography pool is concentrated using, for example, a diafiltration unit.

A binding partner, such as an inhibitor, may then be added to the purified sample. The binding partner is particularly useful in stabilizing the TACE polypeptide. The binding partner may be any suitable compound. Suitable binding partners include, for example, hydroxamate-based inhibitors. One suitable inhibitor is N-{D,L-2-(hydroxyaminocarbonyl)methyl-4-methylpentanoyl}-L-3-amino-2-dimethylbutanoyl-L-alanine, 2-(amino)ethyl amide. This inhibitor, as well as other inhibitors, are described in US patent No. 5,594,106 (Black *et al.*), herein incorporated in its entirety by reference.

The protein complex can be stored at low temperature, for example, at about 4 °C.

#### TACE Crystal and Methods of Crystallization of TACE Polypeptides

One aspect of the invention relates to a method of crystallizing a TACE polypeptide. A preferred method comprises co-crystallizing a TACE polypeptide with a binding partner described above. Exemplary means for obtaining the TACE polypeptide, as well as purification of the polypeptide are described above.

Crystals may be grown or formed by any suitable method, including drop vapor diffusion, batch, liquid bridge, and dialysis, and under any suitable conditions. Crystallization by drop vapor diffusion is often preferable. In addition, those of skill in the art will appreciate that the crystallization conditions may be varied. Various methods of crystallizing polypeptides are generally known in the art. See, for example, WO 95/35367, WO 97/15588, EP 646 599 A2, GB 2 306 961 A, and WO 97/08300.

In one embodiment of the invention, a DNA construct comprising TACE residues 1-477, with Ser266 changed to Ala, Asn452 changed to Gln, and the sequence Gly-Ser-(His)<sub>6</sub> (SEQ ID NO: 2) added to the C-terminus, may be expressed in CHO cells. These cells primarily secrete a processed mixture of TACE, about half

beginning with Val212 and about half with Arg215. The mixture is purified as described above. The purified TACE polypeptide, with the added binding partner, is stored in a buffer as described above.

The TACE polypeptide and binding partner are co-crystallized. The TACE/binding partner solution, at a polypeptide concentration of about 5 mg/mL to about 12 mg/mL in a TACE buffer described above, is mixed with a suitable crystallization buffer and crystallized using a suitable crystallization technique, for example drop vapor diffusion. Suitable crystallization buffers, for example, include: 0.1 M Na Acetate pH 5.3, 0.2 M CaCl<sub>2</sub>, 30% v/v Ethanol; 0.1 M Na Citrate pH 5.0, 40% v/v Ethanol; 0.1 M Na Citrate pH 8.7, 20% w/v PEG 4000, 20% v/v Isopropanol; and 0.1 M Na Citrate pH 5.4, 20% w/v PEG 4000, 20% v/v Isopropanol. The sample is incubated at a temperature ranging from about 4 to 20 degrees Celsius. A crystalline precipitate is formed.

Seeds from the crystalline precipitate obtained, as whole crystals or crushed crystal suspensions, are transferred, along with a suitable crystallization promoter, such as hair of rabbit, to a solution of concentrated TACE/substrate in a crystallization buffer. Crystals suitable for X-ray data collection are formed.

Another aspect of the invention relates to a TACE polypeptide crystal. One such crystal comprises a TNF- $\alpha$  converting enzyme catalytic domain (TCD) polypeptide co-crystallized with an inhibitor. The crystal diffracts to about 2 Å and belongs to the monoclinic space group P2<sub>1</sub>. The crystal's unit cell comprises four crystallographically independent TCD molecules. The TCD molecules are in an asymmetric unit and are not clustered into separate tetrameres, but are integrated into the infinite periodic structure. The crystal has the cell constants: a=61.38 Å (angstrom), b=126.27 Å, C=81.27 Å and  $\beta$ =107.41°.

#### X-Ray Diffraction

Another aspect of the invention relates to the structure of TACE, particularly the structure of the TACE catalytic domain (TCD). The structure of TACE can be determined utilizing a crystal comprising a TACE polypeptide as described above.



According to the present invention, the structure of TACE, and particularly the TCD, is determined using X-ray crystallography. Any suitable X-ray diffraction method for obtaining three-dimensional structural coordinates of a polypeptide may be used. The three-dimensional structure coordinates, or any part thereof that characterizes the part of the TACE polypeptide of interest, such as the TACE catalytic domain or part thereof that is capable of cleaving the peptide PLAQAVRSSS (SEQ ID NO: 1), can be used as described herein.

#### Methods of Using TACE X-Ray Diffraction Coordinates

The invention also relates to use of the structure coordinates obtained from the above described X-ray diffraction studies of the TACE catalytic domain. The coordinates may be utilized, by direct analysis, with the aide of computers, or combinations thereof, to determine the structure, including secondary and tertiary structure, of the TACE catalytic domain. The TACE catalytic domain structure coordinates also may be used to develop, design, and/or screen compounds that associate with TACE. As used herein, "associate" means that the compound may bind to or interact with TACE ionically, covalently, by hydrogen bond, van der Waals interaction, salt bridges, steric interaction, hydrophilic interactions and hydrophobic interaction. Moreover, the term "associate" encompasses associations with any portion of the TACE catalytic domain. For example, compounds that associate with TACE may be compounds that act as competitive inhibitors, un-competitive inhibitors, and non-competitive inhibitors. Compounds that associate with TACE also may be compounds that act as mediators or other regulatory compounds. Compounds that associate with TACE also may be compounds that isomerize to short-lived reaction intermediates in the chemical reaction of substrate with TACE. In particular, compounds designed to associate with TACE may be used therapeutically as inhibitors, mediators and other regulatory compounds.

The use of X-ray coordinates for structure determination, molecular design and selection and synthesis of compounds that associate with other polypeptides is known in the art. Published PCT application WO 95/35367 describes the use of X-

ray structure coordinates to design, evaluate, synthesize and use compounds that associate with the active site of an enzyme. UK Patent Application 2306961A describes the use of X-ray coordinates in rational drug design. Published PCT application, WO 97/15588 describes the structural determination of a polypeptide using x-ray diffraction patterns as well as use of the coordinates and three-dimensional structure in finding compounds that associate with the polypeptide of interest. This invention, however, for the first time allows the use of X-ray coordinates for a TACE polypeptide for structural determination, molecular design, and selection and synthesis of compounds that associate with TACE.

In one aspect of the invention, the structure coordinates obtained by the foregoing methods may be displayed as, or converted to, a graphical representation, including three-dimensional shape representations. This may be accomplished using commercially available computer programs capable of generating graphical representations of molecules, or parts thereof, from a set of structural coordinates. Examples of computer programs capable of generating graphical representations of molecules, or parts thereof, from a set of structural coordinates are described in published PCT application WO 97/08300, incorporated in the entirety by reference.

In another aspect of the invention, the structure coordinates and structure may be compared to, or superimposed over, other similar molecules, such as other metalloproteinases. For example, the TACE structure coordinates and structure may be compared to or superimposed over the structure coordinates or structure of snake venom metalloproteinases, such as, for example, adamalysin II. The TACE structure coordinates and structure also may be compared to or superimposed over the structure coordinates or structure of matrix metalloproteinases, such as ADAM 10, including human ADAM 10. Comparison of TACE and other molecules for which a graphical structure or three-dimensional structural coordinates are available may be carried out with the aid of available software applications, such as the Molecular Similarity application of QUANTA (Molecular Simulations, Inc., Waltham, MA).

Compounds that associate with TACE also may be computationally evaluated and designed by screening and selecting chemical entities or fragments for their

ability to associate with TACE, and specifically the TACE catalytic domain. Several methods may be used to accomplish this aspect of the invention. In one embodiment, one may visually inspect a computer-generated model of TACE, and specifically the catalytic domain, based on the structure coordinates described herein. Computer generated models of chemical entities or specific chemical moieties can then be positioned in or around the catalytic domain and evaluated based on energy minimization and molecular dynamics, using, for example, available programs such as CHARMM or AMBER. Positioning of the chemical entity or fragment can be accomplished, for example with docking software such as Quanta and Sybyl. Additionally, known and commercially available computer programs may be used in selecting chemical entities or fragments. Once suitable chemical entities or fragments are selected, they may be assembled into a single compound, such as an inhibitor, mediator, or other regulatory compound. Known and commercially available model building software may assist in assembly.

In one aspect of the invention, compounds that associate with TACE and specifically the TACE catalytic domain may be designed as a whole, rather than by assembly of specific chemical moieties or chemical entities. This embodiment may be carried out using computer programs such as LUDI (Biosym Technologies, San Diego, CA), LEGEND (Molecular Simulations, Burlington, MA), and Leap Frog (Tripos Associates, St. Louis, MO).

In one embodiment, a candidate compound is chosen based upon the desired sites of interaction with TACE and the candidate compound in light of the sites of interaction identified previously. Once the specific candidate compound-TACE interactions are determined, docking studies, using commercially available docking software, are performed to provide preliminary “modeled” complexes of selected candidate compound with TACE.

Constrained conformational analysis is performed using, for example, molecular dynamics (MD) to check the integrity of the modeled TACE-inhibitor complex. Once the complex reaches its most favorable conformational state, the structure as proposed by the MD study is analyzed visually to ensure that the modeled

complex complies with known experimental SAR/QSAR (structure-activity relationship/quantitative structure-activity relationship) based on measured binding affinities.

Other modeling techniques also may be used in accordance with the invention. Examples of these techniques are disclosed in Cohen *et al.*, "Molecular Modeling Software and Methods for Medicinal Chemistry," *J. Med. Chem.*, 33:883-894 (1990) and Navia *et al.*, "The Use of Structural Information in Drug Design," *Current Opinions in Structural Biology*, 2:202-210 (1992), herein incorporated by reference in the entirety.

Compounds developed or designed to associate with TACE may be optimized or the efficiency of association can be tested using a number of methods known in the art. For example, the deformation energy and electrostatic interactions may be determined and optimized. Known and commercially available software and hardware systems may be used. Structure-based analoging for optimization of the inhibitor potency, selectivity and physical drug-like properties in an iterative manner also may be performed by one skilled in the art of drug design.

Substitutions also may be made to selected or designed compounds. These substitutions can be made to improve or modify the association properties of the compound. Such substitutions may be made, for example, in side groups or particular atoms of the compounds. Generally, one should begin with conservative substitutions that have approximately the same size, shape, charge and other characteristics of the original group or atom. Substituted compounds may be further analyzed and optimized as described above.

In a further aspect of the invention, the potential inhibitory, mediatory, regulatory, or other binding effect of a compound may be analyzed and evaluated, using, for example, commercially available computer software, prior to actual synthesis and testing of such compound. In this way, one can evaluate the probability of synthesizing and testing of inoperative compounds.

Procedures for measuring inhibition generally are known in the art and are disclosed, for example, in PCT 96/41624. Such methods include assays based on reaction with a peptide substrate.

5     TACE Catalytic Domain Structure

The physical features of the TCD, determined based on the X-ray diffraction data obtained using the methods described and its use in creating molecular models of the TCD, are further described, with reference to the Figures.

10     The domain depicted in Fig. 1 has the shape of an oblate ellipsoid, notched at its flat side to give a relatively small active-site cleft separating the small “lower” subdomain from the “upper” main molecular body (Fig. 2a). The TCD polypeptide chain starts on the molecular surface (in the lower back, Fig. 1), with the chain becoming well defined between Asp217 and Met221 (see Fig. 3). Central to the molecule is the five-stranded  $\beta$ -pleated sheet, with the  $\beta$ -strands arranged in the order  
15     (from back to front, see Fig 1) sII, sI, sIII, sV and sIV (see Fig. 3), with sIV, the “edge” strand, running antiparallel to the others. This  $\beta$ -sheet is highly twisted flanked by two  $\alpha$ -helices (hB and hB2) on its convex and two helices (hA and hC) on its concave side. The  $\beta$ -strands sI and sII are connected by the short  $\alpha$ -helix hA1 and the long  $\alpha$ -helix hA (the obliquely running helix on the backside, Fig. 1). The  $\beta$ -  
20     strands sII and sIII are linked by the large “multiple-turn loop”, the long “intermediate”  $\alpha$ -helix hB and the adjacent short  $\alpha$ -helix hB2, all of them arranged on “top” of the  $\beta$ -sheet thus fully shielding its central part from bulk water (Fig. 1). The multiple-turn loop is bulged out at two sites giving rise to a “spur-like” and a quite acidic protuberance, respectively (visible in Fig. 2a on top of the molecule).  
25     The sIII-sIV linker terminates in a short “bulge”, before it enters the edge strand sIV. The sIV-sV connecting segment is dissected into two large “ear-like” surface-located loops, a first one nestling to the main molecular body (giving rise to the “blue” surface, center left, in Fig. 2a), and a long  $\beta$ -hairpin loop (sIIa-sIIb) projecting from the molecular surface (top left in Figs. 1 and 2). A bulged-out loop links sV with the

“active-site helix” hC, which is located in the center of the molecule and stops abruptly at the strictly conserved Gly412, where the chain kinks down to build the lower subdomain.

The C-terminal chain comprising the last 61 TCD residues (Fig. 3) first forms three short straight almost perpendicularly arranged segments linked by two “narrow” supertwisted loops, returns via the tight “Met-turn” Tyr433-Val434-Met435-Tyr436 (SEQ ID NO: 10) back to the surface where it kinks at Pro437 to form the Pro437-Ile438-Ala439 outer “wall” of the S1’ crevice, approaches in a wide loop the C-terminal  $\alpha$ -helix hD and runs through it, and ends up on the molecular “back” surface close to the N-terminus, with the last defined residues Arg473-Ser474 fixed via hydrogen bonds to the main molecular body. Via Cys423-Cys453, the first of the two “narrow” loops is disulfide-linked with the N-terminus of helix hD, whose C-terminal end in turn is clamped to the “ear-like” sIV-sV linker peptide through Cys365-Cys469. Spatially adjacent, the third disulfide bridge of TCD, Cys225-Cys333, connects the N-terminal parts of  $\beta$ -strands sI and sIII. In the intact TACE molecule, four residues downstream of Ser474 would reside Cys478, which is already integral part of the compact elongated disintegrin domain (Saudek *et al.*, “Three-dimensional structure of echistatin, the smallest active RGD protein” *Biochem.* 30, 7369-7372 (1991)). Considering Ser474 and this Cys478 as pivot points of their respective domains, the three residue linker would allow relatively unconstrained docking of the disintegrin domain to the “left” surface side of the catalytic domain.

The active-site cleft of TACE (Fig. 2a) is relatively flat on the left hand (non-primed) side, but becomes notched towards the right. The catalytic zinc residing in its center is penta-coordinated by the three imidazole N $\epsilon$ 2 atoms of His405, His409 and His415 (provided by the active-site helix and the following “descending” chain comprising the conserved zinc binding consensus motif HEXXHXXGXXH) (SEQ ID NO: 3), and by the carbonyl and the hydroxyl oxygen of the hydroxamic acid moiety of the inhibitor (see Figs. 1, 2a and 4). This zinc-imidazole ensemble is based on the distal  $\epsilon$ -methyl-sulphur moiety of the strictly conserved Met435, harbored in the Met-turn characteristic for the metzincin clan (Bode *et al.*, “Astacins, serralysins, snake

venom and matrix metalloproteinases exhibit identical zinc binding environments (HEXXHXXGXXH (SEQ ID NO: 3) and Met-turn) and topologies and should be grouped into a common family, the ‘metzincins’” *FEBS Lett.* 331, 134-140 (1993); Stöcker *et al.*, “The metzincins: Topological and sequential relations between the  
5 astacins, adamalysins, serralysins, and matrixins (collagenases) define a superfamily of zinc-peptidases” *Protein Sci.* 4, 823-840 (1995)). Both carboxylate oxygens of the “catalytic” Glu4O6 (which acts as a general base during catalysis (Grams *et al.*, “X-ray structures of human neutrophil collagenase complexed with peptide hydroxamate and peptide thiol inhibitors: Implications for substrate binding and rational drug  
10 design” *Eur. J. Biochem.* 228, 830-841 (1995)) squeezed between the zinc-liganding imidazole of His4O5 and the edge strand, are hydrogen bonded to the hydroxyl and the N-H group of the hydroxamic acid (see Fig. 4). To the right of the catalytic zinc opens the deep S1’ pocket, which, besides the S1’ wall-forming segment (bottom, Figs. 1 and 2a), is bordered by the side chains of His4O5 and Glu4O6 (left), the sIV  
15 main chain and the Leu345 side chain (top), and the side chains of Val44O (back) and Ala439 (right). To the right of Ala439 opens a second (S3’) pocket, which inside the molecule merges with the S1’ pocket, leaving a small bridge made of the opposing side chains of Ala439 and Leu348 (Fig. 2a).

The (pseudo)peptidic part of the inhibitor binds in an extended geometry to the  
20 notched right-hand side of the active-site cleft, mimicking the interaction of the primed residues of a productively bound peptide substrate (Fig. 2a). It runs antiparallel to the upper short bulge Gly346-Thr347-Leu348 and parallel to the S1’ wall-forming segment Pro437-Ile438-Ala439, making two and two inter-main chain hydrogen bonds, respectively. The dominant intermolecular interactions are made by  
25 the P1’ isobutyl (pseudo-leucyl) side chain of the inhibitor and the essentially hydrophobic S1’ pocket, however, is large and accommodates three partially ordered solvent molecules in addition. The P2’ t-butyl side chain extends away from the enzyme, but nestles to the hydrophobic canopy above formed by the enzyme’s bulge. The P3’ Ala side chain points into the large negatively charged S3’ pocket, but is too

short to make favorable contacts. The C-terminal diaminoethyl group has different conformations in the four molecules.

The P1' to P3' segment Val77-Arg78-Ser79 of a bound pro-TNF $\alpha$  probably binds in a similar manner, possibly under better matching with the underlying cleft surface; the preceding P3 to P1 residues Ala74-Gln75-Ala76 certainly will align antiparallel to the edge strand, with their side chains extending into the (partially charged) S3 pocket and the (negatively charged) shallow S2 depression, and projecting out of the central cleft, respectively. The primed subsites and surrounding molecular surfaces of TACE are dominated by negative charges, while the non-primed subsites are essentially hydrophobic in nature (Fig. 2a). More distant interactions may be involved in the specificity of TACE for processing pro-TNF $\alpha$ . The 12 residue substrate comprising the pro-TNF $\alpha$  cleavage site can also be split by some of the MMPs, although with less specificity and efficacy (Black *et al.*, "Relaxed specificity of matrix metalloproteinases (MMPs) and TIMP intensity of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) production suggest the major TNF- $\alpha$  converting enzyme is not an MMP" *Biochem. Biophys. Res. Commun.* 225, 400-405 (1996)). Thus, the preferential processing of the (probably trimeric) (Tang *et al.*, "Human pro-tumor necrosis factor is a homotrimer" *Biochem.* 35, 8216-8225 (1996a); Tang *et al.*, "Length of the linking domain of human pro-tumor necrosis factor determines the cleavage processing" *Biochem.* 35, 8226-8233 (1996b)) membrane-bound pro-TNF $\alpha$  in *vivo* might in part be due to correct assembling, i.e. suitable presentation of the pro-TNF $\alpha$  cleavage segment to the TACE active site in a distinct distance from the anchoring membrane. Some experimental evidence (Tang *et al.*, *Biochem.* 35, 8216-8225 (1996a); Tang *et al.*, *Biochem.* 35, 8226-8233 (1996b)) suggests that the cleavage site might not be determined by the cleavage sequence alone, but that also the distance to the base of the compact cone formed by the associated C-terminal segments of three TNF $\alpha$  molecules (Jones *et al.*, "Structure of tumor necrosis factor" *Nature* 338, 225-228 (1989)) plays a role. In a productive TACE-proTNF $\alpha$  complex, the base of this TNF $\alpha$ -trimer cone (into which the disordered N-termini run up) may



be recognized by the “right” side of the TACE catalytic domain (Fig. 2a), with the about 10 residues long spacer favoring the correct placement of the proTNF $\alpha$  Ala76-Val77 scissile peptide bond in the active site of TACE.

The polypeptide topology and in particular the surface presentation of the catalytic zinc prove the catalytic domain of TACE to be a typical metzincin. (Bode *et al.*, “Astacins, serralysins, snake venom and matrix metalloproteinases exhibit identical zinc binding environments (HEXXHXXGXXH (SEQ ID NO: 3) and Met-turn) and topologies and should be grouped into a common family, the ‘metzincins’” *FEBS lett.* 331, 134-140 (1993); Stöcker *et al.*, “The metzincins: Topological and sequential relations between the astacins, adamalysins, serralysins, and matrixins (collagenases) define a superfamily of zinc-peptidases” *Protein Sci.* 4, 823-840 (1995)) A superposition with the other metzincins shows, however, that its topology is most similar to that of the catalytic domain of snake venom metalloproteinases such as adamalysin II (Fig. 5). (Gomis-Rüth *et al.*, “First structure of a snake venom metalloproteinase: prototype for matrix metalloproteinases/collagenases” *EMBO J.* 12, 4151-4157 (1993); Zhang *et al.*, “Structural interaction of natural and synthetic inhibitors with the venom metalloproteinase, atrolysin C (form d)” *Proc. Natl. Acad. Sci. USA* 91, 8447-8451 (1994); Kumasaka *et al.*, “Crystal structure of H2-proteinase from the venom of *Trimeresurus flavoviridis*” *J. Biochem.* 119, 49-57 (1996)) This close homology is reflected by the much better simultaneous superposition of the central sheet and the large helices, but in particular also by a couple of structural features, which TACE shares exclusively with the adamalysins such as: the long helix hB and the preceding multiple-turn loop arranged on top of the  $\beta$ -sheet; the typically arranged and shaped C-terminal helix hC; and the extended C-terminus placed on the backside surface. About 175 of the 263 TACE and 201 adamalysin  $\alpha$ -atoms are topologically equivalent (with an rms deviation of 1.3 Å, 39 of which have identical side chains (Fig. 3). These numbers are close to those obtained from a comparison of members within the different metzincin families. (Stöcker *et al.*, *supra*) In addition, detailed structural features prove the close relationship of TACE to the adamalysins: a more conserved core structure; the loosely arranged N-terminus; the characteristic

Asp416 (directly following the zinc binding consensus motif, Fig. 3) involved in identical intramolecular hydrogen bond interactions; the adjacent disulfide bridge Cys423-Cys453 linking the first narrow loop to the C-terminal helix hD (which TACE does not share with adamalysin II, but with the H2-proteinase from the snake venom of *T. flavoviridis*) (Kumasaka *et al.*, *supra*); disulfide bridge Cys365-Cys469 connecting the sIV-sV linker with the C-terminal helix hD; a similarly shaped active-site cleft, with particularly strong similarities in the S1' pocket and other primed subsites.

The catalytic domain of TACE (TCD) also differs from adamalysin II in several respects: with 263 residues, its chain is much longer; most of the additional residues of TACE are clustered giving rise to a more projecting hA-sII turn, to the two surface protuberances of the multiple-turn loop, to the two "ears" of the sIV-sV linker, and to a more bulged-out sV-hC connector (see Figs. 3 and 5); lack of a calcium binding site but presence of a third disulfide bridge Cys225-Cys333 in TACE, both elements serving, however, for the same function namely to clamp the N-terminal chain to strand sill; the quite deep S3' pocket of TACE which merges with its S1' pocket; an almost inverted charge pattern in and around the primed subsites, with an absolute predominance of positive charges in adamalysin.

According to its sequence, and probably with respect to its three-dimensional structure, the TACE catalytic domain is thus not a typical member of the mammalian ADAMs proper (a family of membrane-anchored cell-surface proteins, with the catalytic domain quite homologous to adamalysin (Wolfsberg *et al.*, "ADAMs in Fertilization and Development" *Developm. Biol.* 180, 389-401 (1996))) TACE presumably shares this "outsider" role with (bovine) ADAM 10 (Fig. 3), which does also possess some TACE-like activity (Lunn *et al.*, "Purification of ADAM 10 from bovine spleen as a TNF $\alpha$  convertase," *FEBS Lett.* 400, 333-335 (1997)), and whose *Drosophila* version (*kuz*) has recently been shown to process the Notch receptor (Rooke *et al.*, *Science* 273, 1227-1231 (1996)). Also ADAM 10 probably exhibits an elongated hA-sII loop and the two "ears" typical for TACE, but might have a multiple-turn intermediate in size between TACE and adamalysin (see Fig. 3). Ninety

of the ADAM 10 catalytic domain residues are identical to TACE further underlining the close homology (see Fig. 3), whereas the other mammalian ADAMs probably resemble much more adamalysin II (Gomis-Ruth *et al.*, “Refined 2.0 Å crystal structure of snake venom zinc endopeptidase adamalysin II” *J. Mol. Biol.* 239, 513-544 (1994)).

The structural homology of TACE to the MMPs is significantly lower. The relative arrangement of the common secondary structural elements differs more (reflected by the significantly larger rms deviation of 1.6 Å of the about 120 topologically equivalent C $\alpha$ -atoms), and the MMPs lack characteristic TACE/adamalysin structural elements (such as the intermediate helix hB and the multiple-turn loop, the Asp residue behind the third zinc-binding histidine), or exhibit typical determinants (such as the structural zinc and the integrated calcium ions) not seen in TACE. Notwithstanding the differences in secondary structure, the active-site cleft of TACE bears some similarity with that of the MMPs, with the flat nonprimed (left-hand) side, and the narrow primed side centering in the deep S1' pocket (Fig. 2b). This subsite similarity to the MMPs explains the observed partial sensitivity of TNF $\alpha$ -convertase activity towards synthetic hydroxamic acid inhibitors originally designed for inhibition of various MMPs (DiMartino *et al.*, “Anti-arthritis activity of hydroxamic acid-based pseudopeptide inhibitors of matrix metalloproteinases and TNF $\alpha$  processing” *Inflamm. Res.* 46, 211-215 (1997)). Model building experiments with TIMP-1 structure (Gomis-Ruth *et al.*, “Mechanism of inhibition of the human matrix metalloproteinase stromelysin-1 by TIMP-1” *Nature* 389, 77-81(1997)) show no obvious obstacles in the active-site region of TACE that would easily explain its resistance to blockage by the TIMPs.

This TCD crystal structure thus gives evidence for a topological similarity of the catalytic domain of TACE with that of the adamalysins/ADAMs, and for a share of its substrate binding site to that of the MMPs. TACE exhibits, however, several structural peculiarities regarding surface contour, charge and shape, which facilitates the design of potent selective synthetic inhibitors.

In designing and developing compounds, such as inhibitors, mediators and other compounds having activities with biological significance, that associate with TACE, it is desirable to select compounds with a view toward the particular surface contour, charge, shape, and other physical characteristics of the TACE catalytic domain. Generally, the compounds should be capable of physically and structurally associating with TACE, as well as be able to assume a conformation that allows it to associate with TACE. The features described above will direct the skilled artisan in this regard. In particular, compounds with a linear functionality should be particularly suitable. Such compounds will be particularly suitable in light of the deep pockets of the TACE catalytic domain.

The compounds that associate with TACE, for example, may be designed to associate with the S1' region or the S1'S3' pocket of TACE. Compounds that associate with TACE also may be designed to (i) incorporate a moiety that chelates zinc. Further exemplary compounds include compounds are designed to form a hydrogen bond with Leu348 or Gly349 of TACE, (ii) introduce a non-polar group which occupies the S1' pocket of TACE, (iii) introduce a group which lies within the channel joining S1' - S3' pockets of TACE and which makes appropriate van der Waal contact with the channel, and (iv) form a hydrogen bond with Leu348 or Gly349 on the backbone amide groups of TNF- $\alpha$ -converting enzyme, or (v) any combination of the above.

### Computer-Readable Medium

The present invention also relates to a computer-readable medium having recorded thereon the x-ray diffraction structure coordinates of a crystalline TACE polypeptide. The computer-readable media of the invention are useful for storage, transfer, and use with software of the TACE structural coordinates. The computer readable medium may be any suitable data storage material, including, but not limited to, a floppy disc, a hard disc, computer-type Random Access Memory, Read-Only Memory flash memory, CD-ROM, recordable and rewritable CDs, recordable and rewritable DVDs, magnetic-optical disk, ZIP drive, JAZ drive, Syquest drive, digital tape drive, or the like. Other suitable media will be known to those of skill in the art.

In one embodiment, the computer readable medium comprises the coordinates of Table 1 or a substantial portion thereof. The computer-readable medium may be used in conjunction with a machine programmed with instructions for using the data recorded on the medium, such as a computer loaded with one or more programs identified throughout the specification, to display a graphical, three-dimensional representation of a TACE polypeptide, or any part thereof.

### Computer Based System

Figure 6 illustrates a system 1000 for studying a TACE polypeptide. The system includes a video memory 110 that stores information representing at least a portion of a TACE polypeptide. The memory has at least one first-type storage region 112, having recorded thereon a set of spatial coordinates specifying a location in a three dimensional space, and at least one second-type storage region 114, having recording thereon information representing a characteristic of one of a plurality of amino acids. The second-type storage regions are logically associated with the first-type storage regions in the video memory 110 to represent a geometric arrangement of at least one characteristic of at least a portion of the TACE polypeptide in the three dimensional space. Memory, 112 and 114 can comprise, for example, the data shown in Table 1. The system 1000 also includes a processor, coupled to the memory to access the first-type storage regions 112 and the second-type storage regions 114, to

generate image signals for depicting a visual three dimensional image of at least one characteristic of at least a portion of the TACE polypeptide in the three dimensional space based on data from the memory 110. The processor can be any general purpose processor with a CPU, register, memory and the like. A display 130 coupled to the processor 120 via lines 125 to receive the image signals, for depicting a visual three dimensional image of at least one characteristic of at least a portion of the TACE polypeptide in the three dimensional space based on the image data on a screen 132.

In one embodiment of the invention, the image data includes data for depicting a visual three dimensional image of a ribbon structure of at least a portion of a TACE polypeptide in three dimensional space, such as shown in Fig. 1. In another embodiment, the image data includes data for depicting a visual three dimensional image of a solid model representation of at least a portion of said TACE polypeptide in three dimensional space, such as shown in Fig. 2. In still another embodiment, the image data includes data for depicting a visual three dimensional image of electrostatic surface potential of at least a portion of TACE polypeptide in three dimensional space, such as shown in Fig. 2. In yet another embodiment, the image data includes data for depicting a visual three dimensional stereo image of at least a portion of a TACE polypeptide in three dimensional space, such as shown in fig. 4.

The system 1000 of the present invention may further comprise a storage device 145 that stores data representing a geometric arrangement of a characteristic of a composition other than the TACE polypeptide and an operator interface, such as a mouse 135, for receiving instructions from a operator. Storage device 145 can include, for example, the three-dimensional X-ray coordinate data for other chemical entities. The processor 120 is coupled to the storage device 145 and to said operator interface 135 and generates additional image data for depicting the geometric arrangement of the characteristic of the composition relative to said visual three dimensional image of said at least one characteristic of said at least a portion of TACE polypeptide on the screen 132 based on instructions from the operator interface. In the Fig. 6 embodiment, the storage device 145 is part of the memory 110.

The first-type storage regions 112 and said second-type storage regions 114 are regions of, for example, a semiconductor memory, regions of an optical disk, or regions of a magnetic memory.

In one embodiment, processor 120 and video memory 110 are in the form of a  
 5 UNIX or VAX computer, such those available from Silicon Graphics, Sun Microsystems, and IBM. However, the invention is not limited to use of this particular hardware and software.

The invention is described in more detail in the following illustrative examples. Although the examples may represent only selected embodiments of the  
 10 invention, it should be understood that the following examples are illustrative and not limiting.

#### Example 1 - TACE Polypeptide Expression, Isolation, and Purification

A cDNA encoding the signal peptide, pro and catalytic domains of TACE,  
 15 amino acid residues 1-477 (SEQ ID NO: 8), as disclosed in Black et al., "A Metalloproteinase disintegrin that releases tumour-necrosis factor- $\alpha$  from cells," *Nature* 385: 729-733 (Feb. 1997), with Ser266 changed to Ala, Asn452 changed to Gln and the sequence Gly-Ser-(His)<sub>6</sub> (SEQ ID NO: 2) added to the C-terminus, was inserted into an expression vector for CHO cells. The TACE polypeptide was  
 20 expressed in CHO cells and a mixture of the TACE polypeptide beginning either with Val212 or Arg215 was secreted. The cells were cultured in the drug, methotrexate, which kills those cells that did not incorporate the vector.

The expressed TACE polypeptide was then purified. Purification started with 5 liters of the medium containing the expressed TACE polypeptide. The medium was  
 25 concentrated to about 200 mL with a Millipore 10K cut-off, 1 ft<sup>2</sup> TFF diafiltration unit. The pumping rate was 50-100 mL/min. Two liters of a buffer solution of 20 mM Tris (pH 7.5) and 300 mM NaCl (Buffer E) was then added to the sample.

The sample was reconcentrated as described above and diluted a second time with 2 liters of Buffer E, reconcentrated again, diluted a third time with 2 liters of  
 30 Buffer E, and reconcentrated to about 100 mL. The sample retained in the

diafiltration unit was recovered by a back-flush. This material was then filtered through a 0.45  $\mu\text{m}$  and was azide added to 0.05%. The filtered sample was stored overnight at 4 °C.

5 After overnight storage, imidazole was added to the filtered sample to 5 mM from a 200 mM stock in water and  $\text{ZnCl}_2$  was added to 5  $\mu\text{M}$  from a 1 M stock in water. The sample then was pumped over 2.2 mL of Qiagen Ni-NTA Superflow resin (Cat. # 30430) at 3 mL/min (column size 7.5 x 50 mm).

10 The column was washed at 5 mL/min with 100 mL of a buffer of 20 mM Tris pH 7.5, 300 mM NaCl, 5 mM imidazole, and 5  $\mu\text{M}$   $\text{ZnCl}_2$  (Buffer A). The protein was then eluted with an increasing gradient of imidazole, going up to 200 mM in 1 minute (5 mL total volume), followed by 35 mL of 200 mM imidazole in Buffer A. Two mL fractions were collected, TACE generally coming off about 6 mL into the elution. The fractions were collected in tubes containing 500  $\mu\text{L}$  of 50% glycerol in water and 200  $\mu\text{L}$  of 1 M Tris pH 8. The glycerol in water was prepared the day of the column  
15 run.

A dot blot, with 3  $\mu\text{L}$  from each fraction, was stained with amido black to determine which fractions contained a significant amount of protein. The fractions with a significant amount of protein were pooled. The pool was then concentrated to 1-2 mL with a 10 K cut-off Amicon Centriprep concentrator.

20 The inhibitor N-{D,L-2-(hydroxyaminocarbonyl)methyl-4-methylpentanoyl}-L-3-amino-2-dimethylbutanoyl-L-alanine, 2-(amino)ethyl amide was added to the concentrated sample to 1 mM from a 50 mM stock in water, and octylglucoside was added to 1% from a 10% stock in water. The sample was then incubated at room temperature for 15-24 hours.

25 Following incubation, the sample was applied to a 21.5 x 600 mm size exclusion column, LKB 2135-365, packed with TSK-G3000 SWG, and equilibrated with 10 mM Tris pH 7.5, 100 mM NaCl, 10% glycerol. This buffer was then pumped through the column at 2.5 mL/min for 100 minutes. The TACE polypeptide in the effluent was detected by absorption at 280 nm. Excluded material generally eluted at  
30 about 38 minutes. The pure TACE generally eluted at about 78 minutes or longer.



A gel analysis, with 15 µl of all fractions with significant protein was then carried out to determine which fractions should be pooled. The size-exclusion chromatography pool was concentrated to about 1 mL with a 10 K cut-off Amicon Centriprep concentrator.

5           The inhibitor N-{D,L-2-(hydroxyaminocarbonyl)methyl-4-methylpentanoyl}-L-3-amino-2-dimethylbutanoyl-L-alanine, 2-(amino)ethyl amide was then added to the purified sample to a concentration of 1 mM. The protein can be stored at 4 °C.

#### Example 2 - Protein Crystallization

10           A DNA construct comprising the prodomain and the catalytic domain of human TACE (residues 1-477) was fused to the sequence Gly-Ser-(His)<sub>6</sub> (SEQ ID NO: 2) to facilitate purification of the protein on a Ni-NTA affinity column. Chinese Hamster Ovary (CHO) cells were used for protein expression. The cells secreted a mixture of mature TACE beginning with either Val212 or Arg215. TACE-containing  
15           fractions from the Ni-NTA column were incubated in a buffer containing octylglucoside and the binding partner N-[D,L-2-(hydroxyaminocarbonyl)methyl]-4-methyl-pentanoyl-L-3-(tert-butyl)-glycyl-L-alanine. The final purification step was performed on a gel filtration column. Purified TACE was stored in a buffer containing 10 mM Tris/HCL pH 7.5, 100 mM NaCl, 10% glycerol and 1 mM of  
20           inhibitor (TACE buffer).

Crystallization experiments were set up at a TACE concentration of approximately 5 mg/mL by mixing TACE (in TACE buffer) in a 1:1 ratio with the crystallization buffers listed below and using the sitting drop vapor diffusion technique. The experiments were performed in duplicate and incubated either at  
25           about 4°C or at 20°C. Crystalline precipitate was obtained at 20°C in the following crystallization buffers:

- |           |  |
|-----------|--|
| Buffer A) | 0.1 M Na Acetate pH 5.3, 0.2 M CaCl <sub>2</sub> , 30% v/v Ethanol |
| Buffer B) | 0.1 M Na Citrate pH 5.0, 40% v/v Ethanol                           |
| Buffer C) | 0.1 M Na Citrate pH 8.7, 20% w/v PEG 4000, 20% v/v Isopropanol     |

Small crystals were obtained upon transferring seeds from the crystalline precipitate with a hair of a rabbit into a 1:1 mixture of a concentrated sample of TACE (12 mg/mL in TACE buffer) with either buffer B or C. Further refinement of buffer C resulted in buffer D, which allowed the production of crystals suitable for X-ray data collection.

Buffer D) 0.1 M Na Citrate pH 5.4, 20% w/v PEG 4000, 20% v/v Isopropanol

The first data set was measured to a reduction of 2.5 Å on a MAR300 imaging plate scanner attached to a Rigaku-Denki totaling Cu-anode generator operated at 5.4 kW providing graphite-monochromatized CuK $\alpha$  radiation. The data were processed with MOSFLM v. 5.23 program and routines of the CCP4 suite. All attempts to solve the structure by molecular replacement methods using either adamalysin II, an all-alanine model of adamalysin II and models generated failed to produce useful starting points for phasing. Thus the locations of four independent zinc atoms were determined with the help of an anomalous difference Patterson synthesis. In order to measure MAD data, the crystals were deep-frozen in liquid nitrogen. Therefore, crystals were transferred into a cryo buffer (80% v/v buffer D containing 17% v/v glycerol) with the help of a silk loop of appropriate size, soaked for about 10 seconds and then immediately deep-frozen at 90 degrees K.

The crystals obtained belong to the monoclinic space group P2<sub>1</sub>, have cell constants  $a = 61.38$  Å (angstrom),  $b = 126.27$  Å,  $c = 81.27$  Å,  $\beta = 107.41^\circ$ , and contain four molecules in the asymmetric unit.

### Example 3 - X-ray Diffraction

Using the crystals described in Example 2, a first data set was measured to a resolution of 2.5 Å on a MAR300 imaging plate scanner attached to a Rigaku-Denki rotating Cu-anode generator operated at 5.4kW providing graphite-monochromatized CuK $\alpha$  radiation. The data were processed at with the MOSFLM v. 5.23 program and routines of the CCP4 suite.

All attempts to solve the structure by molecular replacement methods using either adamalysin II, an all-alanine model of adamalysin II, and other models failed to produce useful starting points for phasing.

Thus, the locations of the four independent zinc atoms were determined with the help of an anomalous difference Patterson synthesis. In order to measure MAD data, the crystals were deep-frozen in a nitrogen gas stream cooled down to the temperature of liquid nitrogen. The crystals were first transferred into a cryo-buffer of 80% v/v Buffer D (0.1 M Na Citrate pH 5.4, 20% w/v PEG 4000, 20% v/v Isopropanol) containing 17% v/v glycerol. Transfer to the cryo-buffer was performed with the help of a silk loop of appropriate size. The crystals were soaked in the cryo-buffer for about 10 seconds and then immediately deep-frozen at 90 K.

Anomalous diffraction data to 2.0 Å were collected with MAR345 imaging plate scanner at 90 K on the BW6 wiggler beamline of DORIS (DESY, Hamburg, Germany), using monochromatic X-ray radiation at the wavelengths of maximal  $f''$  (1.2769 Å) and minimal  $f''$  (1.2776 Å) at the K absorption edge of zinc and at a remote wavelength (1.060 Å). The data were scanned and evaluated using DENZO/SCALEPACK, yielding 77653 independent reflections from 1051836 measurements (96.9% completeness, R-merge 0.031 in intensities).

MAD phases were refined and calculated with MLPHARE including all measured data to 2.0 Å resolution. Their initial mean-figure-of-merit of 0.53 was increased to 0.76 by solvent flattening/histogram matching methods applying DM. This density allowed building of the complete chains of the four independent TACE catalytic domains and the bound hydroxamic acid substrates on an SGI system using TURBO-FRODO. This model was crystallographically refined with XPLOR and

with CCP4 routines to a crystallographic R factor of 18.6% ( $R_{\text{free}}$  27.4%) using 79400 independent reflections from, 12.0 to 2Å. resolution.

Four independent TACE molecules form the periodic arrangement.

5 Molecules 1 and 2, and 3 and 4 are defined from Asp219 and Met221, respectively, to Ser474.

#### Example 4 - X-ray Diffraction

10 Anomalous dispersion diffraction data to 2.0 Å were collected with a MAR345 imaging plate scanner at 100 K on the wiggler beamline of DORIS (DESY, Hamburg, Germany), using monochromatic X-ray radiation of maximal  $f'$  (1.2797 Å) and minimal  $f'$  (1.2804 Å) at the K absorption edge of zinc and at a remote wavelength (1.060 Å). These data were evaluated and scanned using DENZO/SCALEPACK, yielding 77,653 independent reflections (96.9% completeness, R-merge 0.031).

15 The structure coordinates obtained are reproduced in Table 1.

Table 1

REMARK Created by MOLEMAN V. 961218/7.2.5 at Fri Sep 19 20:05:05 1997 for user carlos

REMARK MoleMan PDB file

|        |          |          |          |       |          |       |      |   |
|--------|----------|----------|----------|-------|----------|-------|------|---|
| CRYST1 | 61.387   | 126.278  | 81.273   | 90.00 | 107.42   | 90.00 | P 21 | 4 |
| ORIGX1 | 1.000000 | 0.000000 | 0.000000 |       | 0.000000 |       |      |   |
| ORIGX2 | 0.000000 | 1.000000 | 0.000000 |       | 0.000000 |       |      |   |
| ORIGX3 | 0.000000 | 0.000000 | 1.000000 |       | 0.000000 |       |      |   |
| SCALE1 | 0.016290 | 0.000000 | 0.005111 |       | 0.000000 |       |      |   |
| SCALE2 | 0.000000 | 0.007919 | 0.000000 |       | 0.000000 |       |      |   |
| SCALE3 | 0.000000 | 0.000000 | 0.012896 |       | 0.000000 |       |      |   |

|      | Atom | Type | Residue | Z | #   | X     | Y      | Z      | OCC  | B     |
|------|------|------|---------|---|-----|-------|--------|--------|------|-------|
| ATOM | 1    | N    | ASP     | A | 219 | 0.865 | 33.077 | 15.204 | 1.00 | 20.00 |
| ATOM | 2    | OD2  | ASP     | A | 219 | 5.154 | 33.868 | 14.335 | 1.00 | 20.00 |
| ATOM | 3    | OD1  | ASP     | A | 219 | 4.450 | 35.924 | 14.844 | 1.00 | 20.00 |
| ATOM | 4    | CG   | ASP     | A | 219 | 4.191 | 34.718 | 14.461 | 1.00 | 20.00 |
| ATOM | 5    | CB   | ASP     | A | 219 | 2.738 | 34.303 | 14.156 | 1.00 | 20.00 |
| ATOM | 6    | CA   | ASP     | A | 219 | 2.290 | 33.026 | 14.883 | 1.00 | 20.00 |
| ATOM | 7    | C    | ASP     | A | 219 | 3.166 | 32.889 | 16.123 | 1.00 | 20.00 |
| ATOM | 8    | O    | ASP     | A | 219 | 3.439 | 33.884 | 16.819 | 1.00 | 20.00 |
| ATOM | 9    | N    | PRO     | A | 220 | 3.629 | 31.679 | 16.386 | 1.00 | 20.00 |
| ATOM | 10   | CG   | PRO     | A | 220 | 4.073 | 29.436 | 16.118 | 1.00 | 20.00 |
| ATOM | 11   | CD   | PRO     | A | 220 | 3.224 | 30.531 | 15.588 | 1.00 | 20.00 |
| ATOM | 12   | CB   | PRO     | A | 220 | 4.893 | 29.974 | 17.303 | 1.00 | 20.00 |
| ATOM | 13   | CA   | PRO     | A | 220 | 4.523 | 31.452 | 17.495 | 1.00 | 20.00 |
| ATOM | 14   | C    | PRO     | A | 220 | 5.649 | 32.530 | 17.443 | 1.00 | 20.00 |
| ATOM | 15   | O    | PRO     | A | 220 | 6.513 | 32.741 | 18.173 | 1.00 | 20.00 |
| ATOM | 16   | N    | MET     | A | 221 | 5.766 | 33.341 | 16.625 | 1.00 | 48.83 |
| ATOM | 17   | CE   | MET     | A | 221 | 9.090 | 36.336 | 12.584 | 1.00 | 53.01 |
| ATOM | 18   | SD   | MET     | A | 221 | 9.248 | 36.147 | 14.337 | 1.00 | 54.21 |
| ATOM | 19   | CG   | MET     | A | 221 | 8.515 | 34.606 | 14.801 | 1.00 | 51.15 |
| ATOM | 20   | CB   | MET     | A | 221 | 7.101 | 34.778 | 15.298 | 1.00 | 48.69 |
| ATOM | 21   | CA   | MET     | A | 221 | 6.875 | 34.306 | 16.701 | 1.00 | 46.22 |
| ATOM | 22   | C    | MET     | A | 221 | 6.485 | 35.500 | 17.614 | 1.00 | 42.51 |
| ATOM | 23   | O    | MET     | A | 221 | 7.279 | 36.002 | 18.427 | 1.00 | 43.93 |
| ATOM | 24   | N    | LYS     | A | 222 | 5.215 | 35.817 | 17.508 | 1.00 | 36.53 |
| ATOM | 25   | NZ   | LYS     | A | 222 | 1.844 | 39.934 | 13.657 | 1.00 | 40.05 |
| ATOM | 26   | CE   | LYS     | A | 222 | 2.513 | 39.901 | 14.974 | 1.00 | 39.09 |
| ATOM | 27   | CD   | LYS     | A | 222 | 2.353 | 38.522 | 15.613 | 1.00 | 38.20 |
| ATOM | 28   | CG   | LYS     | A | 222 | 3.646 | 38.146 | 16.312 | 1.00 | 36.27 |
| ATOM | 29   | CB   | LYS     | A | 222 | 3.345 | 37.404 | 17.597 | 1.00 | 33.97 |
| ATOM | 30   | CA   | LYS     | A | 222 | 4.567 | 36.853 | 18.299 | 1.00 | 32.39 |
| ATOM | 31   | C    | LYS     | A | 222 | 4.144 | 36.220 | 19.633 | 1.00 | 29.13 |
| ATOM | 32   | O    | LYS     | A | 222 | 2.999 | 35.844 | 19.866 | 1.00 | 26.54 |
| ATOM | 33   | N    | ASN     | A | 223 | 5.157 | 36.011 | 20.462 | 1.00 | 23.62 |
| ATOM | 34   | CA   | ASN     | A | 223 | 4.951 | 35.295 | 21.704 | 1.00 | 22.97 |
| ATOM | 35   | CB   | ASN     | A | 223 | 5.756 | 33.987 | 21.611 | 1.00 | 25.44 |
| ATOM | 36   | CG   | ASN     | A | 223 | 7.229 | 34.245 | 21.372 | 1.00 | 26.32 |
| ATOM | 37   | OD1  | ASN     | A | 223 | 7.973 | 33.261 | 21.243 | 1.00 | 29.74 |
| ATOM | 38   | ND2  | ASN     | A | 223 | 7.688 | 35.482 | 21.319 | 1.00 | 25.96 |
| ATOM | 39   | C    | ASN     | A | 223 | 5.327 | 36.123 | 22.908 | 1.00 | 18.46 |
| ATOM | 40   | O    | ASN     | A | 223 | 5.365 | 35.556 | 23.983 | 1.00 | 18.08 |
| ATOM | 41   | N    | THR     | A | 224 | 5.611 | 37.408 | 22.709 | 1.00 | 17.03 |

|      | Atom | Type | Residue | ? | #   | X      | Y      | Z      | OCC  | B     |
|------|------|------|---------|---|-----|--------|--------|--------|------|-------|
| ATOM | 42   | CA   | THR     | A | 224 | 6.035  | 38.246 | 23.824 | 1.00 | 16.24 |
| ATOM | 43   | CB   | THR     | A | 224 | 7.507  | 38.721 | 23.599 | 1.00 | 17.52 |
| ATOM | 44   | OG1  | THR     | A | 224 | 8.317  | 37.590 | 23.318 | 1.00 | 16.14 |
| ATOM | 45   | CG2  | THR     | A | 224 | 8.002  | 39.440 | 24.840 | 1.00 | 17.72 |
| ATOM | 46   | C    | THR     | A | 224 | 5.152  | 39.464 | 24.033 | 1.00 | 16.13 |
| ATOM | 47   | O    | THR     | A | 224 | 4.863  | 40.275 | 23.152 | 1.00 | 15.14 |
| ATOM | 48   | N    | CYS     | A | 225 | 4.708  | 39.650 | 25.253 | 1.00 | 16.61 |
| ATOM | 49   | CA   | CYS     | A | 225 | 3.915  | 40.833 | 25.646 | 1.00 | 17.81 |
| ATOM | 50   | CB   | CYS     | A | 225 | 2.895  | 40.460 | 26.723 | 1.00 | 18.01 |
| ATOM | 51   | SG   | CYS     | A | 225 | 2.120  | 41.843 | 27.562 | 1.00 | 18.77 |
| ATOM | 52   | C    | CYS     | A | 225 | 4.899  | 41.914 | 26.101 | 1.00 | 17.46 |
| ATOM | 53   | O    | CYS     | A | 225 | 5.614  | 41.703 | 27.093 | 1.00 | 18.52 |
| ATOM | 54   | N    | LYS     | A | 226 | 5.070  | 42.945 | 25.285 | 1.00 | 17.94 |
| ATOM | 55   | CA   | LYS     | A | 226 | 6.011  | 44.033 | 25.573 | 1.00 | 18.61 |
| ATOM | 56   | CB   | LYS     | A | 226 | 6.373  | 44.816 | 24.311 | 1.00 | 21.04 |
| ATOM | 57   | CG   | LYS     | A | 226 | 6.985  | 43.974 | 23.202 | 1.00 | 22.16 |
| ATOM | 58   | CD   | LYS     | A | 226 | 8.395  | 43.451 | 23.514 | 1.00 | 24.95 |
| ATOM | 59   | CE   | LYS     | A | 226 | 8.867  | 42.585 | 22.365 | 1.00 | 28.75 |
| ATOM | 60   | NZ   | LYS     | A | 226 | 10.336 | 42.445 | 22.185 | 1.00 | 31.31 |
| ATOM | 61   | C    | LYS     | A | 226 | 5.461  | 44.940 | 26.658 | 1.00 | 17.48 |
| ATOM | 62   | O    | LYS     | A | 226 | 4.295  | 45.336 | 26.642 | 1.00 | 16.96 |
| ATOM | 63   | N    | LEU     | A | 227 | 6.281  | 45.274 | 27.641 | 1.00 | 15.78 |
| ATOM | 64   | CA   | LEU     | A | 227 | 5.848  | 46.025 | 28.777 | 1.00 | 15.23 |
| ATOM | 65   | CB   | LEU     | A | 227 | 6.182  | 45.347 | 30.117 | 1.00 | 15.96 |
| ATOM | 66   | CG   | LEU     | A | 227 | 5.848  | 43.884 | 30.334 | 1.00 | 15.88 |
| ATOM | 67   | CD1  | LEU     | A | 227 | 6.375  | 43.381 | 31.692 | 1.00 | 15.72 |
| ATOM | 68   | CD2  | LEU     | A | 227 | 4.356  | 43.646 | 30.314 | 1.00 | 13.61 |
| ATOM | 69   | C    | LEU     | A | 227 | 6.462  | 47.398 | 28.965 | 1.00 | 16.89 |
| ATOM | 70   | O    | LEU     | A | 227 | 7.639  | 47.635 | 28.725 | 1.00 | 17.35 |
| ATOM | 71   | N    | LEU     | A | 228 | 5.585  | 48.248 | 29.488 | 1.00 | 16.01 |
| ATOM | 72   | CA   | LEU     | A | 228 | 6.024  | 49.559 | 29.935 | 1.00 | 15.78 |
| ATOM | 73   | CB   | LEU     | A | 228 | 5.105  | 50.721 | 29.644 | 1.00 | 15.98 |
| ATOM | 74   | CG   | LEU     | A | 228 | 5.360  | 52.012 | 30.426 | 1.00 | 17.60 |
| ATOM | 75   | CD1  | LEU     | A | 228 | 6.596  | 52.712 | 29.853 | 1.00 | 15.81 |
| ATOM | 76   | CD2  | LEU     | A | 228 | 4.154  | 52.945 | 30.340 | 1.00 | 19.40 |
| ATOM | 77   | C    | LEU     | A | 228 | 6.144  | 49.360 | 31.455 | 1.00 | 16.70 |
| ATOM | 78   | O    | LEU     | A | 228 | 5.124  | 49.074 | 32.104 | 1.00 | 16.99 |
| ATOM | 79   | N    | VAL     | A | 229 | 7.356  | 49.488 | 31.983 | 1.00 | 13.83 |
| ATOM | 80   | CA   | VAL     | A | 229 | 7.484  | 49.343 | 33.450 | 1.00 | 12.75 |
| ATOM | 81   | CB   | VAL     | A | 229 | 8.600  | 48.320 | 33.747 | 1.00 | 15.41 |
| ATOM | 82   | CG1  | VAL     | A | 229 | 9.015  | 48.421 | 35.199 | 1.00 | 15.21 |
| ATOM | 83   | CG2  | VAL     | A | 229 | 8.062  | 46.910 | 33.451 | 1.00 | 16.11 |
| ATOM | 84   | C    | VAL     | A | 229 | 7.758  | 50.710 | 34.055 | 1.00 | 11.45 |
| ATOM | 85   | O    | VAL     | A | 229 | 8.592  | 51.462 | 33.529 | 1.00 | 10.78 |
| ATOM | 86   | N    | VAL     | A | 230 | 7.029  | 51.092 | 35.090 | 1.00 | 11.10 |
| ATOM | 87   | CA   | VAL     | A | 230 | 7.169  | 52.397 | 35.688 | 1.00 | 13.35 |
| ATOM | 88   | CB   | VAL     | A | 230 | 5.910  | 53.299 | 35.518 | 1.00 | 13.78 |
| ATOM | 89   | CG1  | VAL     | A | 230 | 6.096  | 54.643 | 36.192 | 1.00 | 13.70 |
| ATOM | 90   | CG2  | VAL     | A | 230 | 5.577  | 53.586 | 34.050 | 1.00 | 12.14 |
| ATOM | 91   | C    | VAL     | A | 230 | 7.495  | 52.252 | 37.154 | 1.00 | 12.98 |
| ATOM | 92   | O    | VAL     | A | 230 | 6.791  | 51.546 | 37.877 | 1.00 | 14.51 |
| ATOM | 93   | N    | ALA     | A | 231 | 8.582  | 52.891 | 37.570 | 1.00 | 14.57 |
| ATOM | 94   | CA   | ALA     | A | 231 | 8.915  | 52.901 | 39.001 | 1.00 | 12.63 |
| ATOM | 95   | CB   | ALA     | A | 231 | 10.382 | 52.556 | 39.219 | 1.00 | 14.54 |

|      | Atom |         |     |   |     |        |        |        |      |       |
|------|------|---------|-----|---|-----|--------|--------|--------|------|-------|
|      | Type | Residue | Z   | # | X   | Y      | Z      | OCC    | B    |       |
| ATOM | 96   | C       | ALA | A | 231 | 8.616  | 54.305 | 39.505 | 1.00 | 13.54 |
| ATOM | 97   | O       | ALA | A | 231 | 9.215  | 55.290 | 39.004 | 1.00 | 12.89 |
| ATOM | 98   | N       | ASP | A | 232 | 7.739  | 54.412 | 40.500 | 1.00 | 13.89 |
| ATOM | 99   | CA      | ASP | A | 232 | 7.440  | 55.781 | 40.947 | 1.00 | 15.63 |
| ATOM | 100  | CB      | ASP | A | 232 | 6.061  | 55.875 | 41.560 | 1.00 | 16.03 |
| ATOM | 101  | CG      | ASP | A | 232 | 5.856  | 55.198 | 42.876 | 1.00 | 17.24 |
| ATOM | 102  | OD1     | ASP | A | 232 | 4.725  | 55.249 | 43.432 | 1.00 | 18.20 |
| ATOM | 103  | OD2     | ASP | A | 232 | 6.804  | 54.565 | 43.403 | 1.00 | 15.69 |
| ATOM | 104  | C       | ASP | A | 232 | 8.559  | 56.276 | 41.875 | 1.00 | 15.96 |
| ATOM | 105  | O       | ASP | A | 232 | 9.395  | 55.459 | 42.253 | 1.00 | 13.21 |
| ATOM | 106  | N       | HIS | A | 233 | 8.375  | 57.492 | 42.392 | 1.00 | 16.98 |
| ATOM | 107  | CA      | HIS | A | 233 | 9.399  | 58.118 | 43.244 | 1.00 | 16.61 |
| ATOM | 108  | CB      | HIS | A | 233 | 9.075  | 59.600 | 43.522 | 1.00 | 17.60 |
| ATOM | 109  | CG      | HIS | A | 233 | 7.977  | 59.866 | 44.494 | 1.00 | 17.74 |
| ATOM | 110  | CD2     | HIS | A | 233 | 8.012  | 60.040 | 45.836 | 1.00 | 18.92 |
| ATOM | 111  | ND1     | HIS | A | 233 | 6.648  | 59.946 | 44.152 | 1.00 | 17.72 |
| ATOM | 112  | CE1     | HIS | A | 233 | 5.910  | 60.144 | 45.222 | 1.00 | 18.19 |
| ATOM | 113  | NE2     | HIS | A | 233 | 6.730  | 60.214 | 46.266 | 1.00 | 19.56 |
| ATOM | 114  | C       | HIS | A | 233 | 9.562  | 57.364 | 44.535 | 1.00 | 16.98 |
| ATOM | 115  | O       | HIS | A | 233 | 10.626 | 57.385 | 45.170 | 1.00 | 14.73 |
| ATOM | 116  | N       | ARG | A | 234 | 8.457  | 56.762 | 45.005 | 1.00 | 16.26 |
| ATOM | 117  | CA      | ARG | A | 234 | 8.476  | 55.997 | 46.231 | 1.00 | 16.71 |
| ATOM | 118  | CB      | ARG | A | 234 | 7.083  | 55.600 | 46.688 | 1.00 | 19.19 |
| ATOM | 119  | CG      | ARG | A | 234 | 6.078  | 56.729 | 46.814 | 1.00 | 18.94 |
| ATOM | 120  | CD      | ARG | A | 234 | 4.726  | 56.181 | 47.250 | 1.00 | 21.89 |
| ATOM | 121  | NE      | ARG | A | 234 | 3.696  | 57.214 | 47.125 | 1.00 | 23.72 |
| ATOM | 122  | CZ      | ARG | A | 234 | 2.872  | 57.469 | 48.130 | 1.00 | 26.70 |
| ATOM | 123  | NH1     | ARG | A | 234 | 2.923  | 56.798 | 49.270 | 1.00 | 27.34 |
| ATOM | 124  | NH2     | ARG | A | 234 | 1.953  | 58.411 | 47.989 | 1.00 | 28.96 |
| ATOM | 125  | C       | ARG | A | 234 | 9.319  | 54.728 | 46.062 | 1.00 | 17.39 |
| ATOM | 126  | O       | ARG | A | 234 | 10.072 | 54.359 | 46.955 | 1.00 | 17.02 |
| ATOM | 127  | N       | PHE | A | 235 | 9.149  | 54.039 | 44.954 | 1.00 | 15.45 |
| ATOM | 128  | CA      | PHE | A | 235 | 9.913  | 52.829 | 44.669 | 1.00 | 17.15 |
| ATOM | 129  | CB      | PHE | A | 235 | 9.458  | 52.167 | 43.370 | 1.00 | 15.92 |
| ATOM | 130  | CG      | PHE | A | 235 | 10.063 | 50.804 | 43.165 | 1.00 | 14.51 |
| ATOM | 131  | CD1     | PHE | A | 235 | 11.226 | 50.638 | 42.442 | 1.00 | 14.09 |
| ATOM | 132  | CD2     | PHE | A | 235 | 9.429  | 49.693 | 43.697 | 1.00 | 13.27 |
| ATOM | 133  | CE1     | PHE | A | 235 | 11.786 | 49.394 | 42.283 | 1.00 | 12.49 |
| ATOM | 134  | CE2     | PHE | A | 235 | 9.979  | 48.436 | 43.514 | 1.00 | 14.15 |
| ATOM | 135  | CZ      | PHE | A | 235 | 11.159 | 48.280 | 42.812 | 1.00 | 11.73 |
| ATOM | 136  | C       | PHE | A | 235 | 11.391 | 53.211 | 44.502 | 1.00 | 15.85 |
| ATOM | 137  | O       | PHE | A | 235 | 12.309 | 52.611 | 45.041 | 1.00 | 15.02 |
| ATOM | 138  | N       | TYR | A | 236 | 11.573 | 54.282 | 43.750 | 1.00 | 15.65 |
| ATOM | 139  | CA      | TYR | A | 236 | 12.920 | 54.781 | 43.501 | 1.00 | 18.77 |
| ATOM | 140  | CB      | TYR | A | 236 | 12.809 | 56.087 | 42.744 | 1.00 | 20.15 |
| ATOM | 141  | CG      | TYR | A | 236 | 14.079 | 56.831 | 42.453 | 1.00 | 20.77 |
| ATOM | 142  | CD1     | TYR | A | 236 | 15.006 | 56.379 | 41.554 | 1.00 | 23.25 |
| ATOM | 143  | CE1     | TYR | A | 236 | 16.171 | 57.111 | 41.294 | 1.00 | 25.10 |
| ATOM | 144  | CD2     | TYR | A | 236 | 14.303 | 58.043 | 43.094 | 1.00 | 22.97 |
| ATOM | 145  | CE2     | TYR | A | 236 | 15.434 | 58.789 | 42.840 | 1.00 | 23.38 |
| ATOM | 146  | CZ      | TYR | A | 236 | 16.355 | 58.309 | 41.944 | 1.00 | 24.28 |
| ATOM | 147  | OH      | TYR | A | 236 | 17.490 | 59.032 | 41.699 | 1.00 | 27.10 |
| ATOM | 148  | C       | TYR | A | 236 | 13.668 | 55.005 | 44.807 | 1.00 | 18.41 |
| ATOM | 149  | O       | TYR | A | 236 | 14.785 | 54.538 | 44.979 | 1.00 | 17.82 |

|      | Atom | Type | Residue | Z | #   | X      | Y      | Z      | OCC  | B     |
|------|------|------|---------|---|-----|--------|--------|--------|------|-------|
| ATOM | 150  | N    | ARG     | A | 237 | 13.029 | 55.671 | 45.741 | 1.00 | 18.84 |
| ATOM | 151  | NH2  | ARG     | A | 237 | 16.164 | 60.578 | 45.801 | 1.00 | 36.66 |
| ATOM | 152  | NH1  | ARG     | A | 237 | 15.513 | 58.642 | 46.822 | 1.00 | 35.42 |
| ATOM | 153  | CZ   | ARG     | A | 237 | 15.208 | 59.704 | 46.106 | 1.00 | 35.99 |
| ATOM | 154  | NE   | ARG     | A | 237 | 13.940 | 59.862 | 45.712 | 1.00 | 36.11 |
| ATOM | 155  | CD   | ARG     | A | 237 | 12.867 | 58.910 | 45.981 | 1.00 | 32.12 |
| ATOM | 156  | CG   | ARG     | A | 237 | 12.655 | 58.442 | 47.386 | 1.00 | 28.99 |
| ATOM | 157  | CB   | ARG     | A | 237 | 12.578 | 56.978 | 47.698 | 1.00 | 22.94 |
| ATOM | 158  | CA   | ARG     | A | 237 | 13.566 | 56.021 | 47.029 | 1.00 | 21.89 |
| ATOM | 159  | C    | ARG     | A | 237 | 13.824 | 54.847 | 47.959 | 1.00 | 22.82 |
| ATOM | 160  | O    | ARG     | A | 237 | 14.874 | 54.759 | 48.586 | 1.00 | 22.33 |
| ATOM | 161  | N    | TYR     | A | 238 | 12.826 | 53.995 | 48.165 | 1.00 | 20.93 |
| ATOM | 162  | CA   | TYR     | A | 238 | 12.807 | 52.950 | 49.142 | 1.00 | 22.79 |
| ATOM | 163  | CB   | TYR     | A | 238 | 11.438 | 52.835 | 49.835 | 1.00 | 25.02 |
| ATOM | 164  | CG   | TYR     | A | 238 | 11.052 | 54.133 | 50.502 | 1.00 | 28.43 |
| ATOM | 165  | CD1  | TYR     | A | 238 | 10.191 | 55.011 | 49.873 | 1.00 | 30.38 |
| ATOM | 166  | CE1  | TYR     | A | 238 | 9.827  | 56.214 | 50.439 | 1.00 | 32.45 |
| ATOM | 167  | CD2  | TYR     | A | 238 | 11.570 | 54.501 | 51.729 | 1.00 | 30.38 |
| ATOM | 168  | CE2  | TYR     | A | 238 | 11.228 | 55.709 | 52.309 | 1.00 | 32.79 |
| ATOM | 169  | CZ   | TYR     | A | 238 | 10.384 | 56.572 | 51.647 | 1.00 | 33.85 |
| ATOM | 170  | OH   | TYR     | A | 238 | 10.043 | 57.784 | 52.208 | 1.00 | 34.86 |
| ATOM | 171  | C    | TYR     | A | 238 | 13.222 | 51.579 | 48.683 | 1.00 | 22.48 |
| ATOM | 172  | O    | TYR     | A | 238 | 13.682 | 50.772 | 49.509 | 1.00 | 24.69 |
| ATOM | 173  | N    | MET     | A | 239 | 13.171 | 51.306 | 47.405 | 1.00 | 20.92 |
| ATOM | 174  | CA   | MET     | A | 239 | 13.680 | 50.048 | 46.893 | 1.00 | 18.57 |
| ATOM | 175  | CB   | MET     | A | 239 | 12.667 | 49.374 | 45.965 | 1.00 | 18.57 |
| ATOM | 176  | CG   | MET     | A | 239 | 11.394 | 48.971 | 46.729 | 1.00 | 18.44 |
| ATOM | 177  | SD   | MET     | A | 239 | 11.677 | 47.664 | 47.929 | 1.00 | 17.64 |
| ATOM | 178  | CE   | MET     | A | 239 | 12.084 | 46.309 | 46.855 | 1.00 | 16.38 |
| ATOM | 179  | C    | MET     | A | 239 | 14.975 | 50.292 | 46.121 | 1.00 | 17.52 |
| ATOM | 180  | O    | MET     | A | 239 | 15.826 | 49.422 | 46.133 | 1.00 | 16.58 |
| ATOM | 181  | N    | GLY     | A | 240 | 15.067 | 51.440 | 45.447 | 1.00 | 16.74 |
| ATOM | 182  | CA   | GLY     | A | 240 | 16.198 | 51.733 | 44.602 | 1.00 | 16.82 |
| ATOM | 183  | C    | GLY     | A | 240 | 17.334 | 52.497 | 45.232 | 1.00 | 20.60 |
| ATOM | 184  | O    | GLY     | A | 240 | 18.280 | 52.875 | 44.516 | 1.00 | 20.21 |
| ATOM | 185  | N    | ARG     | A | 241 | 17.242 | 52.871 | 46.503 | 1.00 | 20.89 |
| ATOM | 186  | CA   | ARG     | A | 241 | 18.300 | 53.628 | 47.162 | 1.00 | 24.17 |
| ATOM | 187  | CB   | ARG     | A | 241 | 19.609 | 52.806 | 47.126 | 1.00 | 26.15 |
| ATOM | 188  | CG   | ARG     | A | 241 | 19.504 | 51.488 | 47.875 | 1.00 | 29.48 |
| ATOM | 189  | CD   | ARG     | A | 241 | 20.771 | 50.648 | 47.896 | 1.00 | 31.73 |
| ATOM | 190  | NE   | ARG     | A | 241 | 21.417 | 50.785 | 49.228 | 1.00 | 32.75 |
| ATOM | 191  | CZ   | ARG     | A | 241 | 22.188 | 51.837 | 49.428 | 1.00 | 33.64 |
| ATOM | 192  | NH1  | ARG     | A | 241 | 22.361 | 52.722 | 48.450 | 1.00 | 35.35 |
| ATOM | 193  | NH2  | ARG     | A | 241 | 22.752 | 52.014 | 50.598 | 1.00 | 32.64 |
| ATOM | 194  | C    | ARG     | A | 241 | 18.497 | 55.001 | 46.543 | 1.00 | 25.05 |
| ATOM | 195  | O    | ARG     | A | 241 | 19.574 | 55.585 | 46.696 | 1.00 | 21.63 |
| ATOM | 196  | N    | GLY     | A | 242 | 17.470 | 55.529 | 45.831 | 1.00 | 22.70 |
| ATOM | 197  | CA   | GLY     | A | 242 | 17.603 | 56.784 | 45.110 | 1.00 | 20.94 |
| ATOM | 198  | C    | GLY     | A | 242 | 18.622 | 56.667 | 44.003 | 1.00 | 20.36 |
| ATOM | 199  | O    | GLY     | A | 242 | 19.255 | 57.656 | 43.639 | 1.00 | 20.42 |
| ATOM | 200  | N    | GLU     | A | 243 | 18.841 | 55.486 | 43.445 | 1.00 | 19.57 |
| ATOM | 201  | CA   | GLU     | A | 243 | 19.832 | 55.277 | 42.418 | 1.00 | 19.51 |
| ATOM | 202  | CB   | GLU     | A | 243 | 20.951 | 54.324 | 42.832 | 1.00 | 21.04 |
| ATOM | 203  | CG   | GLU     | A | 243 | 21.992 | 54.818 | 43.816 | 1.00 | 22.54 |



|      | Atom |         | Z | #   | X      | Y      | Z      | OCC  | B     |
|------|------|---------|---|-----|--------|--------|--------|------|-------|
|      | Type | Residue |   |     |        |        |        |      |       |
| ATOM | 204  | CD GLU  | A | 243 | 22.782 | 53.747 | 44.543 | 1.00 | 24.67 |
| ATOM | 205  | OE1 GLU | A | 243 | 23.740 | 54.097 | 45.292 | 1.00 | 24.23 |
| ATOM | 206  | OE2 GLU | A | 243 | 22.512 | 52.535 | 44.451 | 1.00 | 22.83 |
| ATOM | 207  | C GLU   | A | 243 | 19.104 | 54.717 | 41.197 | 1.00 | 19.62 |
| ATOM | 208  | O GLU   | A | 243 | 18.414 | 53.698 | 41.291 | 1.00 | 18.85 |
| ATOM | 209  | N GLU   | A | 244 | 19.324 | 55.341 | 40.075 | 1.00 | 19.48 |
| ATOM | 210  | CA GLU  | A | 244 | 18.699 | 54.904 | 38.833 | 1.00 | 22.19 |
| ATOM | 211  | CB GLU  | A | 244 | 18.928 | 55.950 | 37.739 | 1.00 | 25.49 |
| ATOM | 212  | CG GLU  | A | 244 | 18.502 | 55.433 | 36.371 | 1.00 | 29.88 |
| ATOM | 213  | CD GLU  | A | 244 | 18.409 | 56.498 | 35.310 | 1.00 | 32.59 |
| ATOM | 214  | OE1 GLU | A | 244 | 18.205 | 57.691 | 35.608 | 1.00 | 33.16 |
| ATOM | 215  | OE2 GLU | A | 244 | 18.528 | 56.090 | 34.136 | 1.00 | 35.02 |
| ATOM | 216  | C GLU   | A | 244 | 19.176 | 53.524 | 38.414 | 1.00 | 21.10 |
| ATOM | 217  | O GLU   | A | 244 | 18.360 | 52.654 | 38.029 | 1.00 | 17.68 |
| ATOM | 218  | N SER   | A | 245 | 20.466 | 53.247 | 38.644 | 1.00 | 18.06 |
| ATOM | 219  | CA SER  | A | 245 | 21.001 | 51.960 | 38.207 | 1.00 | 20.29 |
| ATOM | 220  | CB SER  | A | 245 | 22.549 | 51.953 | 38.270 | 1.00 | 21.06 |
| ATOM | 221  | OG SER  | A | 245 | 22.833 | 52.394 | 39.607 | 1.00 | 21.74 |
| ATOM | 222  | C SER   | A | 245 | 20.409 | 50.844 | 39.056 | 1.00 | 17.46 |
| ATOM | 223  | O SER   | A | 245 | 19.970 | 49.834 | 38.536 | 1.00 | 18.81 |
| ATOM | 224  | N THR   | A | 246 | 20.355 | 51.020 | 40.343 | 1.00 | 15.88 |
| ATOM | 225  | CA THR  | A | 246 | 19.821 | 50.027 | 41.275 | 1.00 | 18.13 |
| ATOM | 226  | CB THR  | A | 246 | 20.051 | 50.546 | 42.689 | 1.00 | 19.42 |
| ATOM | 227  | OG1 THR | A | 246 | 21.459 | 50.877 | 42.861 | 1.00 | 21.14 |
| ATOM | 228  | CG2 THR | A | 246 | 19.692 | 49.547 | 43.761 | 1.00 | 19.86 |
| ATOM | 229  | C THR   | A | 246 | 18.337 | 49.757 | 41.014 | 1.00 | 16.92 |
| ATOM | 230  | O THR   | A | 246 | 17.915 | 48.619 | 41.068 | 1.00 | 14.90 |
| ATOM | 231  | N THR   | A | 247 | 17.545 | 50.799 | 40.800 | 1.00 | 17.19 |
| ATOM | 232  | CA THR  | A | 247 | 16.108 | 50.689 | 40.560 | 1.00 | 16.84 |
| ATOM | 233  | CB THR  | A | 247 | 15.458 | 52.076 | 40.443 | 1.00 | 16.21 |
| ATOM | 234  | OG1 THR | A | 247 | 15.860 | 52.839 | 41.581 | 1.00 | 14.61 |
| ATOM | 235  | CG2 THR | A | 247 | 13.920 | 52.069 | 40.449 | 1.00 | 14.87 |
| ATOM | 236  | C THR   | A | 247 | 15.848 | 49.892 | 39.308 | 1.00 | 15.69 |
| ATOM | 237  | O THR   | A | 247 | 15.088 | 48.922 | 39.295 | 1.00 | 14.94 |
| ATOM | 238  | N THR   | A | 248 | 16.502 | 50.305 | 38.232 | 1.00 | 16.92 |
| ATOM | 239  | CA THR  | A | 248 | 16.382 | 49.685 | 36.926 | 1.00 | 16.92 |
| ATOM | 240  | CB THR  | A | 248 | 17.322 | 50.415 | 35.963 | 1.00 | 17.93 |
| ATOM | 241  | OG1 THR | A | 248 | 16.875 | 51.787 | 35.915 | 1.00 | 18.06 |
| ATOM | 242  | CG2 THR | A | 248 | 17.381 | 49.792 | 34.586 | 1.00 | 19.15 |
| ATOM | 243  | C THR   | A | 248 | 16.712 | 48.202 | 36.972 | 1.00 | 18.22 |
| ATOM | 244  | O THR   | A | 248 | 16.073 | 47.313 | 36.427 | 1.00 | 14.91 |
| ATOM | 245  | N ASN   | A | 249 | 17.857 | 47.907 | 37.593 | 1.00 | 17.46 |
| ATOM | 246  | CA ASN  | A | 249 | 18.342 | 46.545 | 37.700 | 1.00 | 17.81 |
| ATOM | 247  | CB ASN  | A | 249 | 19.723 | 46.472 | 38.349 | 1.00 | 19.11 |
| ATOM | 248  | CG ASN  | A | 249 | 20.854 | 47.016 | 37.499 | 1.00 | 22.53 |
| ATOM | 249  | OD1 ASN | A | 249 | 20.753 | 47.173 | 36.283 | 1.00 | 22.82 |
| ATOM | 250  | ND2 ASN | A | 249 | 21.989 | 47.306 | 38.157 | 1.00 | 21.73 |
| ATOM | 251  | C ASN   | A | 249 | 17.364 | 45.662 | 38.478 | 1.00 | 15.16 |
| ATOM | 252  | O ASN   | A | 249 | 17.157 | 44.510 | 38.066 | 1.00 | 13.94 |
| ATOM | 253  | N TYR   | A | 250 | 16.850 | 46.170 | 39.578 | 1.00 | 14.10 |
| ATOM | 254  | CA TYR  | A | 250 | 15.888 | 45.426 | 40.360 | 1.00 | 15.67 |
| ATOM | 255  | CB TYR  | A | 250 | 15.393 | 46.239 | 41.546 | 1.00 | 16.52 |
| ATOM | 256  | CG TYR  | A | 250 | 14.527 | 45.444 | 42.501 | 1.00 | 19.76 |
| ATOM | 257  | CD1 TYR | A | 250 | 15.109 | 44.778 | 43.571 | 1.00 | 20.38 |

|      | Atom | Type | Residue | Z | #   | X      | Y      | Z      | OCC  | B     |
|------|------|------|---------|---|-----|--------|--------|--------|------|-------|
| ATOM | 258  | CE1  | TYR     | A | 250 | 14.344 | 44.031 | 44.447 | 1.00 | 21.56 |
| ATOM | 259  | CD2  | TYR     | A | 250 | 13.138 | 45.344 | 42.332 | 1.00 | 18.76 |
| ATOM | 260  | CE2  | TYR     | A | 250 | 12.377 | 44.600 | 43.203 | 1.00 | 19.63 |
| ATOM | 261  | CZ   | TYR     | A | 250 | 12.985 | 43.943 | 44.248 | 1.00 | 22.22 |
| ATOM | 262  | OH   | TYR     | A | 250 | 12.250 | 43.189 | 45.134 | 1.00 | 24.91 |
| ATOM | 263  | C    | TYR     | A | 250 | 14.683 | 45.029 | 39.472 | 1.00 | 14.95 |
| ATOM | 264  | O    | TYR     | A | 250 | 14.234 | 43.893 | 39.546 | 1.00 | 11.83 |
| ATOM | 265  | N    | LEU     | A | 251 | 14.133 | 46.021 | 38.758 | 1.00 | 13.07 |
| ATOM | 266  | CA   | LEU     | A | 251 | 12.977 | 45.742 | 37.899 | 1.00 | 12.72 |
| ATOM | 267  | CB   | LEU     | A | 251 | 12.271 | 47.059 | 37.519 | 1.00 | 12.66 |
| ATOM | 268  | CG   | LEU     | A | 251 | 11.696 | 47.800 | 38.734 | 1.00 | 14.96 |
| ATOM | 269  | CD1  | LEU     | A | 251 | 11.038 | 49.099 | 38.363 | 1.00 | 18.53 |
| ATOM | 270  | CD2  | LEU     | A | 251 | 10.717 | 46.914 | 39.501 | 1.00 | 19.00 |
| ATOM | 271  | C    | LEU     | A | 251 | 13.288 | 44.885 | 36.700 | 1.00 | 11.35 |
| ATOM | 272  | O    | LEU     | A | 251 | 12.518 | 43.962 | 36.349 | 1.00 | 10.33 |
| ATOM | 273  | N    | ILE     | A | 252 | 14.429 | 45.093 | 36.050 | 1.00 | 10.29 |
| ATOM | 274  | CA   | ILE     | A | 252 | 14.832 | 44.209 | 34.944 | 1.00 | 12.09 |
| ATOM | 275  | CB   | ILE     | A | 252 | 16.209 | 44.654 | 34.372 | 1.00 | 13.58 |
| ATOM | 276  | CG2  | ILE     | A | 252 | 16.848 | 43.570 | 33.523 | 1.00 | 14.17 |
| ATOM | 277  | CG1  | ILE     | A | 252 | 16.059 | 45.964 | 33.581 | 1.00 | 16.57 |
| ATOM | 278  | CD1  | ILE     | A | 252 | 17.351 | 46.450 | 32.902 | 1.00 | 18.53 |
| ATOM | 279  | C    | ILE     | A | 252 | 14.938 | 42.791 | 35.448 | 1.00 | 10.51 |
| ATOM | 280  | O    | ILE     | A | 252 | 14.592 | 41.830 | 34.755 | 1.00 | 12.14 |
| ATOM | 281  | N    | GLU     | A | 253 | 15.508 | 42.598 | 36.641 | 1.00 | 9.27  |
| ATOM | 282  | CA   | GLU     | A | 253 | 15.743 | 41.263 | 37.159 | 1.00 | 10.71 |
| ATOM | 283  | CB   | GLU     | A | 253 | 16.762 | 41.233 | 38.306 | 1.00 | 12.25 |
| ATOM | 284  | CG   | GLU     | A | 253 | 18.217 | 41.412 | 37.830 | 1.00 | 12.76 |
| ATOM | 285  | CD   | GLU     | A | 253 | 19.215 | 41.029 | 38.924 | 1.00 | 15.62 |
| ATOM | 286  | OE1  | GLU     | A | 253 | 19.091 | 40.009 | 39.615 | 1.00 | 14.92 |
| ATOM | 287  | OE2  | GLU     | A | 253 | 20.134 | 41.798 | 39.207 | 1.00 | 14.69 |
| ATOM | 288  | C    | GLU     | A | 253 | 14.422 | 40.619 | 37.605 | 1.00 | 9.88  |
| ATOM | 289  | O    | GLU     | A | 253 | 14.195 | 39.441 | 37.388 | 1.00 | 7.43  |
| ATOM | 290  | N    | LEU     | A | 254 | 13.559 | 41.420 | 38.230 | 1.00 | 10.47 |
| ATOM | 291  | CA   | LEU     | A | 254 | 12.266 | 40.858 | 38.649 | 1.00 | 10.04 |
| ATOM | 292  | CB   | LEU     | A | 254 | 11.537 | 41.807 | 39.572 | 1.00 | 9.92  |
| ATOM | 293  | CG   | LEU     | A | 254 | 10.103 | 41.493 | 40.022 | 1.00 | 10.99 |
| ATOM | 294  | CD1  | LEU     | A | 254 | 9.778  | 42.322 | 41.239 | 1.00 | 11.71 |
| ATOM | 295  | CD2  | LEU     | A | 254 | 9.106  | 41.854 | 38.918 | 1.00 | 11.46 |
| ATOM | 296  | C    | LEU     | A | 254 | 11.481 | 40.463 | 37.408 | 1.00 | 9.41  |
| ATOM | 297  | O    | LEU     | A | 254 | 10.959 | 39.343 | 37.426 | 1.00 | 10.16 |
| ATOM | 298  | N    | ILE     | A | 255 | 11.399 | 41.269 | 36.369 | 1.00 | 11.15 |
| ATOM | 299  | CA   | ILE     | A | 255 | 10.590 | 40.910 | 35.180 | 1.00 | 11.06 |
| ATOM | 300  | CB   | ILE     | A | 255 | 10.480 | 42.108 | 34.194 | 1.00 | 10.34 |
| ATOM | 301  | CG2  | ILE     | A | 255 | 9.910  | 41.651 | 32.851 | 1.00 | 12.31 |
| ATOM | 302  | CG1  | ILE     | A | 255 | 9.646  | 43.216 | 34.796 | 1.00 | 10.06 |
| ATOM | 303  | CD1  | ILE     | A | 255 | 8.235  | 42.810 | 35.286 | 1.00 | 10.90 |
| ATOM | 304  | C    | ILE     | A | 255 | 11.113 | 39.671 | 34.495 | 1.00 | 11.34 |
| ATOM | 305  | O    | ILE     | A | 255 | 10.466 | 38.704 | 34.055 | 1.00 | 8.95  |
| ATOM | 306  | N    | ASP     | A | 256 | 12.458 | 39.596 | 34.420 | 1.00 | 10.09 |
| ATOM | 307  | CA   | ASP     | A | 256 | 13.108 | 38.362 | 33.953 | 1.00 | 11.00 |
| ATOM | 308  | CB   | ASP     | A | 256 | 14.621 | 38.617 | 33.890 | 1.00 | 12.60 |
| ATOM | 309  | CG   | ASP     | A | 256 | 15.320 | 37.358 | 33.434 | 1.00 | 16.54 |
| ATOM | 310  | OD1  | ASP     | A | 256 | 15.159 | 37.033 | 32.249 | 1.00 | 17.04 |
| ATOM | 311  | OD2  | ASP     | A | 256 | 15.977 | 36.731 | 34.290 | 1.00 | 18.15 |

|      | <u>Atom</u> |                |          |          |          |          |          |            |          |       |
|------|-------------|----------------|----------|----------|----------|----------|----------|------------|----------|-------|
|      | <u>Type</u> | <u>Residue</u> | <u>?</u> | <u>#</u> | <u>X</u> | <u>Y</u> | <u>Z</u> | <u>OCC</u> | <u>B</u> |       |
| ATOM | 312         | C              | ASP      | A        | 256      | 12.763   | 37.124   | 34.779     | 1.00     | 10.53 |
| ATOM | 313         | O              | ASP      | A        | 256      | 12.485   | 36.036   | 34.246     | 1.00     | 11.14 |
| ATOM | 314         | N              | ARG      | A        | 257      | 12.719   | 37.177   | 36.087     | 1.00     | 11.51 |
| ATOM | 315         | CA             | ARG      | A        | 257      | 12.362   | 36.025   | 36.923     | 1.00     | 11.03 |
| ATOM | 316         | CB             | ARG      | A        | 257      | 12.646   | 36.291   | 38.375     | 1.00     | 11.04 |
| ATOM | 317         | CG             | ARG      | A        | 257      | 14.194   | 36.302   | 38.743     | 1.00     | 9.97  |
| ATOM | 318         | CD             | ARG      | A        | 257      | 14.347   | 36.333   | 40.258     | 1.00     | 9.94  |
| ATOM | 319         | NE             | ARG      | A        | 257      | 13.581   | 37.392   | 40.951     | 1.00     | 9.56  |
| ATOM | 320         | CZ             | ARG      | A        | 257      | 14.058   | 38.613   | 41.124     | 1.00     | 10.48 |
| ATOM | 321         | NH1            | ARG      | A        | 257      | 15.283   | 38.961   | 40.677     | 1.00     | 8.64  |
| ATOM | 322         | NH2            | ARG      | A        | 257      | 13.363   | 39.539   | 41.718     | 1.00     | 8.45  |
| ATOM | 323         | C              | ARG      | A        | 257      | 10.868   | 35.673   | 36.655     | 1.00     | 10.99 |
| ATOM | 324         | O              | ARG      | A        | 257      | 10.495   | 34.509   | 36.580     | 1.00     | 10.38 |
| ATOM | 325         | N              | VAL      | A        | 258      | 10.033   | 36.685   | 36.635     | 1.00     | 7.90  |
| ATOM | 326         | CA             | VAL      | A        | 258      | 8.600    | 36.497   | 36.295     | 1.00     | 9.48  |
| ATOM | 327         | CB             | VAL      | A        | 258      | 7.877    | 37.856   | 36.335     | 1.00     | 8.97  |
| ATOM | 328         | CG1            | VAL      | A        | 258      | 6.398    | 37.717   | 35.905     | 1.00     | 7.38  |
| ATOM | 329         | CG2            | VAL      | A        | 258      | 7.915    | 38.447   | 37.733     | 1.00     | 7.76  |
| ATOM | 330         | C              | VAL      | A        | 258      | 8.469    | 35.851   | 34.931     | 1.00     | 9.20  |
| ATOM | 331         | O              | VAL      | A        | 258      | 7.769    | 34.858   | 34.706     | 1.00     | 11.73 |
| ATOM | 332         | N              | ASP      | A        | 259      | 9.193    | 36.330   | 33.947     | 1.00     | 10.44 |
| ATOM | 333         | CA             | ASP      | A        | 259      | 9.196    | 35.817   | 32.585     | 1.00     | 11.92 |
| ATOM | 334         | CB             | ASP      | A        | 259      | 10.101   | 36.614   | 31.655     | 1.00     | 12.64 |
| ATOM | 335         | CG             | ASP      | A        | 259      | 10.059   | 36.157   | 30.219     | 1.00     | 17.49 |
| ATOM | 336         | OD1            | ASP      | A        | 259      | 8.962    | 36.007   | 29.644     | 1.00     | 16.26 |
| ATOM | 337         | OD2            | ASP      | A        | 259      | 11.145   | 35.932   | 29.637     | 1.00     | 20.54 |
| ATOM | 338         | C              | ASP      | A        | 259      | 9.618    | 34.346   | 32.546     | 1.00     | 13.21 |
| ATOM | 339         | O              | ASP      | A        | 259      | 9.021    | 33.572   | 31.783     | 1.00     | 11.13 |
| ATOM | 340         | N              | ASP      | A        | 260      | 10.546   | 33.904   | 33.412     | 1.00     | 12.46 |
| ATOM | 341         | OD2            | ASP      | A        | 260      | 14.081   | 33.042   | 35.067     | 1.00     | 19.42 |
| ATOM | 342         | OD1            | ASP      | A        | 260      | 13.629   | 33.074   | 32.936     | 1.00     | 15.68 |
| ATOM | 343         | CG             | ASP      | A        | 260      | 13.335   | 32.789   | 34.098     | 1.00     | 16.09 |
| ATOM | 344         | CB             | ASP      | A        | 260      | 11.972   | 32.171   | 34.451     | 1.00     | 13.52 |
| ATOM | 345         | CA             | ASP      | A        | 260      | 10.912   | 32.498   | 33.403     | 1.00     | 11.20 |
| ATOM | 346         | C              | ASP      | A        | 260      | 9.647    | 31.669   | 33.761     | 1.00     | 13.45 |
| ATOM | 347         | O              | ASP      | A        | 260      | 9.461    | 30.565   | 33.241     | 1.00     | 11.34 |
| ATOM | 348         | N              | ILE      | A        | 261      | 8.867    | 32.202   | 34.720     | 1.00     | 10.81 |
| ATOM | 349         | CA             | ILE      | A        | 261      | 7.643    | 31.469   | 35.052     | 1.00     | 11.86 |
| ATOM | 350         | CB             | ILE      | A        | 261      | 6.910    | 32.167   | 36.198     | 1.00     | 13.06 |
| ATOM | 351         | CG2            | ILE      | A        | 261      | 5.538    | 31.612   | 36.416     | 1.00     | 12.50 |
| ATOM | 352         | CG1            | ILE      | A        | 261      | 7.825    | 31.986   | 37.422     | 1.00     | 16.02 |
| ATOM | 353         | CD1            | ILE      | A        | 261      | 7.242    | 32.547   | 38.701     | 1.00     | 17.40 |
| ATOM | 354         | C              | ILE      | A        | 261      | 6.738    | 31.396   | 33.815     | 1.00     | 10.07 |
| ATOM | 355         | O              | ILE      | A        | 261      | 6.351    | 30.273   | 33.480     | 1.00     | 11.72 |
| ATOM | 356         | N              | TYR      | A        | 262      | 6.434    | 32.522   | 33.232     | 1.00     | 8.70  |
| ATOM | 357         | CA             | TYR      | A        | 262      | 5.515    | 32.515   | 32.082     | 1.00     | 11.55 |
| ATOM | 358         | CB             | TYR      | A        | 262      | 5.275    | 33.937   | 31.548     | 1.00     | 11.91 |
| ATOM | 359         | CG             | TYR      | A        | 262      | 4.257    | 34.650   | 32.411     | 1.00     | 12.15 |
| ATOM | 360         | CD1            | TYR      | A        | 262      | 4.554    | 35.110   | 33.670     | 1.00     | 12.29 |
| ATOM | 361         | CE1            | TYR      | A        | 262      | 3.598    | 35.746   | 34.457     | 1.00     | 12.53 |
| ATOM | 362         | CD2            | TYR      | A        | 262      | 2.940    | 34.799   | 31.941     | 1.00     | 14.52 |
| ATOM | 363         | CE2            | TYR      | A        | 262      | 1.989    | 35.420   | 32.716     | 1.00     | 14.04 |
| ATOM | 364         | CZ             | TYR      | A        | 262      | 2.315    | 35.905   | 33.956     | 1.00     | 14.14 |
| ATOM | 365         | OH             | TYR      | A        | 262      | 1.368    | 36.538   | 34.724     | 1.00     | 12.39 |

|      | Atom | Type | Residue | ? | #   | X      | Y      | Z      | OCC  | B     |
|------|------|------|---------|---|-----|--------|--------|--------|------|-------|
| ATOM | 366  | C    | TYR     | A | 262 | 5.982  | 31.682 | 30.932 | 1.00 | 11.66 |
| ATOM | 367  | O    | TYR     | A | 262 | 5.202  | 30.842 | 30.446 | 1.00 | 11.39 |
| ATOM | 368  | N    | ARG     | A | 263 | 7.231  | 31.887 | 30.478 | 1.00 | 10.78 |
| ATOM | 369  | CA   | ARG     | A | 263 | 7.771  | 31.180 | 29.333 | 1.00 | 14.61 |
| ATOM | 370  | CB   | ARG     | A | 263 | 9.236  | 31.623 | 29.117 | 1.00 | 18.66 |
| ATOM | 371  | CG   | ARG     | A | 263 | 9.634  | 32.729 | 28.194 | 1.00 | 21.81 |
| ATOM | 372  | CD   | ARG     | A | 263 | 11.103 | 32.655 | 27.718 | 1.00 | 25.82 |
| ATOM | 373  | NE   | ARG     | A | 263 | 11.932 | 31.745 | 28.516 | 1.00 | 27.30 |
| ATOM | 374  | CZ   | ARG     | A | 263 | 12.427 | 32.092 | 29.708 | 1.00 | 28.71 |
| ATOM | 375  | NH1  | ARG     | A | 263 | 12.225 | 33.329 | 30.166 | 1.00 | 29.09 |
| ATOM | 376  | NH2  | ARG     | A | 263 | 13.087 | 31.212 | 30.435 | 1.00 | 27.05 |
| ATOM | 377  | C    | ARG     | A | 263 | 7.751  | 29.674 | 29.425 | 1.00 | 15.13 |
| ATOM | 378  | O    | ARG     | A | 263 | 7.596  | 28.973 | 28.384 | 1.00 | 17.45 |
| ATOM | 379  | N    | ASN     | A | 264 | 8.019  | 29.078 | 30.591 | 1.00 | 12.82 |
| ATOM | 380  | CA   | ASN     | A | 264 | 8.003  | 27.677 | 30.834 | 1.00 | 14.56 |
| ATOM | 381  | CB   | ASN     | A | 264 | 8.878  | 27.204 | 32.013 | 1.00 | 17.95 |
| ATOM | 382  | CG   | ASN     | A | 264 | 10.323 | 27.555 | 31.654 | 1.00 | 19.62 |
| ATOM | 383  | OD1  | ASN     | A | 264 | 10.776 | 27.002 | 30.654 | 1.00 | 23.25 |
| ATOM | 384  | ND2  | ASN     | A | 264 | 10.957 | 28.464 | 32.335 | 1.00 | 19.81 |
| ATOM | 385  | C    | ASN     | A | 264 | 6.582  | 27.144 | 31.076 | 1.00 | 16.00 |
| ATOM | 386  | O    | ASN     | A | 264 | 6.449  | 25.944 | 31.293 | 1.00 | 14.82 |
| ATOM | 387  | N    | THR     | A | 265 | 5.566  | 28.017 | 31.073 | 1.00 | 13.74 |
| ATOM | 388  | CA   | THR     | A | 265 | 4.221  | 27.425 | 31.290 | 1.00 | 13.37 |
| ATOM | 389  | CB   | THR     | A | 265 | 3.309  | 28.463 | 31.935 | 1.00 | 14.37 |
| ATOM | 390  | OG1  | THR     | A | 265 | 3.800  | 28.787 | 33.238 | 1.00 | 11.71 |
| ATOM | 391  | CG2  | THR     | A | 265 | 1.866  | 27.953 | 32.101 | 1.00 | 12.84 |
| ATOM | 392  | C    | THR     | A | 265 | 3.675  | 26.917 | 29.965 | 1.00 | 12.82 |
| ATOM | 393  | O    | THR     | A | 265 | 3.698  | 27.628 | 28.968 | 1.00 | 14.37 |
| ATOM | 394  | N    | ALA     | A | 266 | 3.134  | 25.708 | 29.970 | 1.00 | 13.65 |
| ATOM | 395  | CA   | ALA     | A | 266 | 2.432  | 25.151 | 28.820 | 1.00 | 14.19 |
| ATOM | 396  | CB   | ALA     | A | 266 | 2.737  | 23.645 | 28.812 | 1.00 | 14.17 |
| ATOM | 397  | C    | ALA     | A | 266 | 0.937  | 25.431 | 28.997 | 1.00 | 11.04 |
| ATOM | 398  | O    | ALA     | A | 266 | 0.250  | 24.682 | 29.675 | 1.00 | 10.22 |
| ATOM | 399  | N    | TRP     | A | 267 | 0.426  | 26.539 | 28.524 | 1.00 | 11.35 |
| ATOM | 400  | CA   | TRP     | A | 267 | -0.962 | 26.949 | 28.736 | 1.00 | 13.04 |
| ATOM | 401  | CB   | TRP     | A | 267 | -1.183 | 28.301 | 28.045 | 1.00 | 11.63 |
| ATOM | 402  | CG   | TRP     | A | 267 | -0.186 | 29.330 | 28.523 | 1.00 | 10.70 |
| ATOM | 403  | CD2  | TRP     | A | 267 | -0.205 | 29.920 | 29.819 | 1.00 | 8.77  |
| ATOM | 404  | CE2  | TRP     | A | 267 | 0.904  | 30.814 | 29.863 | 1.00 | 12.19 |
| ATOM | 405  | CE3  | TRP     | A | 267 | -1.007 | 29.828 | 30.931 | 1.00 | 9.72  |
| ATOM | 406  | CD1  | TRP     | A | 267 | 0.865  | 29.846 | 27.849 | 1.00 | 10.38 |
| ATOM | 407  | NE1  | TRP     | A | 267 | 1.531  | 30.754 | 28.652 | 1.00 | 11.35 |
| ATOM | 408  | CZ2  | TRP     | A | 267 | 1.187  | 31.580 | 30.989 | 1.00 | 10.57 |
| ATOM | 409  | CZ3  | TRP     | A | 267 | -0.718 | 30.580 | 32.066 | 1.00 | 11.82 |
| ATOM | 410  | CH2  | TRP     | A | 267 | 0.395  | 31.439 | 32.071 | 1.00 | 9.78  |
| ATOM | 411  | C    | TRP     | A | 267 | -2.007 | 25.919 | 28.298 | 1.00 | 14.01 |
| ATOM | 412  | O    | TRP     | A | 267 | -3.089 | 25.832 | 28.915 | 1.00 | 14.19 |
| ATOM | 413  | N    | ASP     | A | 268 | -1.688 | 25.091 | 27.326 | 1.00 | 11.86 |
| ATOM | 414  | CA   | ASP     | A | 268 | -2.615 | 24.026 | 26.899 | 1.00 | 13.82 |
| ATOM | 415  | CB   | ASP     | A | 268 | -2.765 | 24.051 | 25.382 | 1.00 | 13.92 |
| ATOM | 416  | CG   | ASP     | A | 268 | -1.517 | 23.691 | 24.619 | 1.00 | 16.74 |
| ATOM | 417  | OD1  | ASP     | A | 268 | -0.422 | 23.699 | 25.244 | 1.00 | 16.49 |
| ATOM | 418  | OD2  | ASP     | A | 268 | -1.561 | 23.395 | 23.404 | 1.00 | 15.38 |
| ATOM | 419  | C    | ASP     | A | 268 | -2.165 | 22.661 | 27.367 | 1.00 | 15.26 |

|      | Atom |         | ? | #   | X      | Y      | Z      | OCC  | B     |
|------|------|---------|---|-----|--------|--------|--------|------|-------|
|      | Type | Residue |   |     |        |        |        |      |       |
| ATOM | 420  | O ASP   | A | 268 | -2.554 | 21.608 | 26.834 | 1.00 | 13.18 |
| ATOM | 421  | N ASN   | A | 269 | -1.225 | 22.609 | 28.329 | 1.00 | 14.90 |
| ATOM | 422  | CA ASN  | A | 269 | -0.596 | 21.391 | 28.792 | 1.00 | 15.45 |
| ATOM | 423  | CB ASN  | A | 269 | -1.547 | 20.454 | 29.549 | 1.00 | 17.28 |
| ATOM | 424  | CG ASN  | A | 269 | -2.190 | 21.182 | 30.719 | 1.00 | 18.96 |
| ATOM | 425  | OD1 ASN | A | 269 | -1.464 | 21.670 | 31.560 | 1.00 | 20.34 |
| ATOM | 426  | ND2 ASN | A | 269 | -3.500 | 21.321 | 30.788 | 1.00 | 18.93 |
| ATOM | 427  | C ASN   | A | 269 | 0.108  | 20.556 | 27.711 | 1.00 | 14.79 |
| ATOM | 428  | O ASN   | A | 269 | 0.330  | 19.352 | 27.859 | 1.00 | 14.35 |
| ATOM | 429  | N ALA   | A | 270 | 0.523  | 21.193 | 26.654 | 1.00 | 14.55 |
| ATOM | 430  | CA ALA  | A | 270 | 1.203  | 20.593 | 25.533 | 1.00 | 17.42 |
| ATOM | 431  | CB ALA  | A | 270 | 0.189  | 20.155 | 24.481 | 1.00 | 15.76 |
| ATOM | 432  | C ALA   | A | 270 | 2.239  | 21.573 | 25.004 | 1.00 | 16.67 |
| ATOM | 433  | O ALA   | A | 270 | 3.183  | 21.866 | 25.757 | 1.00 | 19.13 |
| ATOM | 434  | N GLY   | A | 271 | 2.143  | 22.004 | 23.765 | 1.00 | 16.01 |
| ATOM | 435  | CA GLY  | A | 271 | 3.174  | 22.837 | 23.177 | 1.00 | 18.64 |
| ATOM | 436  | C GLY   | A | 271 | 2.951  | 24.321 | 23.125 | 1.00 | 17.56 |
| ATOM | 437  | O GLY   | A | 271 | 3.768  | 25.075 | 22.589 | 1.00 | 18.20 |
| ATOM | 438  | N PHE   | A | 272 | 1.844  | 24.831 | 23.659 | 1.00 | 17.81 |
| ATOM | 439  | CA PHE  | A | 272 | 1.538  | 26.263 | 23.614 | 1.00 | 16.42 |
| ATOM | 440  | CB PHE  | A | 272 | 0.047  | 26.539 | 23.710 | 1.00 | 16.73 |
| ATOM | 441  | CG PHE  | A | 272 | -0.389 | 27.890 | 23.205 | 1.00 | 17.94 |
| ATOM | 442  | CD1 PHE | A | 272 | -0.462 | 28.168 | 21.858 | 1.00 | 19.17 |
| ATOM | 443  | CD2 PHE | A | 272 | -0.716 | 28.894 | 24.100 | 1.00 | 18.80 |
| ATOM | 444  | CE1 PHE | A | 272 | -0.813 | 29.421 | 21.407 | 1.00 | 18.87 |
| ATOM | 445  | CE2 PHE | A | 272 | -1.120 | 30.139 | 23.664 | 1.00 | 18.81 |
| ATOM | 446  | CZ PHE  | A | 272 | -1.142 | 30.404 | 22.310 | 1.00 | 19.11 |
| ATOM | 447  | C PHE   | A | 272 | 2.305  | 26.889 | 24.796 | 1.00 | 16.83 |
| ATOM | 448  | O PHE   | A | 272 | 1.786  | 27.138 | 25.860 | 1.00 | 14.19 |
| ATOM | 449  | N LYS   | A | 273 | 3.584  | 27.067 | 24.561 | 1.00 | 17.93 |
| ATOM | 450  | CA LYS  | A | 273 | 4.522  | 27.543 | 25.546 | 1.00 | 21.35 |
| ATOM | 451  | CB LYS  | A | 273 | 5.236  | 26.296 | 26.080 | 1.00 | 24.32 |
| ATOM | 452  | CG LYS  | A | 273 | 6.157  | 25.698 | 25.023 | 1.00 | 27.94 |
| ATOM | 453  | CD LYS  | A | 273 | 6.625  | 24.300 | 25.389 | 1.00 | 31.29 |
| ATOM | 454  | CE LYS  | A | 273 | 7.307  | 24.300 | 26.732 | 1.00 | 32.80 |
| ATOM | 455  | NZ LYS  | A | 273 | 6.347  | 24.136 | 27.857 | 1.00 | 33.38 |
| ATOM | 456  | C LYS   | A | 273 | 5.479  | 28.518 | 24.906 | 1.00 | 19.96 |
| ATOM | 457  | O LYS   | A | 273 | 5.444  | 28.763 | 23.706 | 1.00 | 18.61 |
| ATOM | 458  | N GLY   | A | 274 | 6.382  | 29.094 | 25.709 | 1.00 | 20.59 |
| ATOM | 459  | CA GLY  | A | 274 | 7.323  | 30.058 | 25.166 | 1.00 | 17.10 |
| ATOM | 460  | C GLY   | A | 274 | 6.701  | 31.449 | 25.153 | 1.00 | 17.80 |
| ATOM | 461  | O GLY   | A | 274 | 7.272  | 32.334 | 24.547 | 1.00 | 17.48 |
| ATOM | 462  | N TYR   | A | 275 | 5.527  | 31.675 | 25.763 | 1.00 | 15.67 |
| ATOM | 463  | CA TYR  | A | 275 | 4.892  | 32.965 | 25.802 | 1.00 | 16.24 |
| ATOM | 464  | CB TYR  | A | 275 | 3.340  | 32.874 | 25.854 | 1.00 | 15.81 |
| ATOM | 465  | CG TYR  | A | 275 | 2.838  | 32.446 | 24.503 | 1.00 | 17.73 |
| ATOM | 466  | CD1 TYR | A | 275 | 2.784  | 31.102 | 24.175 | 1.00 | 17.51 |
| ATOM | 467  | CE1 TYR | A | 275 | 2.384  | 30.722 | 22.919 | 1.00 | 20.42 |
| ATOM | 468  | CD2 TYR | A | 275 | 2.524  | 33.418 | 23.543 | 1.00 | 18.48 |
| ATOM | 469  | CE2 TYR | A | 275 | 2.140  | 33.017 | 22.279 | 1.00 | 20.02 |
| ATOM | 470  | CZ TYR  | A | 275 | 2.065  | 31.690 | 21.989 | 1.00 | 19.42 |
| ATOM | 471  | OH TYR  | A | 275 | 1.670  | 31.304 | 20.737 | 1.00 | 23.70 |
| ATOM | 472  | C TYR   | A | 275 | 5.317  | 33.689 | 27.087 | 1.00 | 15.60 |
| ATOM | 473  | O TYR   | A | 275 | 5.270  | 33.077 | 28.160 | 1.00 | 15.87 |

|      | Atom<br>Type | Residue | ? | #   | X      | Y      | Z      | OCC  | B     |
|------|--------------|---------|---|-----|--------|--------|--------|------|-------|
| ATOM | 474          | N GLY   | A | 276 | 5.638  | 34.959 | 26.991 | 1.00 | 17.04 |
| ATOM | 475          | CA GLY  | A | 276 | 5.978  | 35.692 | 28.190 | 1.00 | 17.48 |
| ATOM | 476          | C GLY   | A | 276 | 5.988  | 37.183 | 28.020 | 1.00 | 19.17 |
| ATOM | 477          | O GLY   | A | 276 | 5.226  | 37.781 | 27.278 | 1.00 | 16.76 |
| ATOM | 478          | N ILE   | A | 277 | 6.893  | 37.805 | 28.811 | 1.00 | 18.66 |
| ATOM | 479          | CA ILE  | A | 277 | 6.938  | 39.245 | 28.907 | 1.00 | 17.89 |
| ATOM | 480          | CB ILE  | A | 277 | 6.413  | 39.745 | 30.256 | 1.00 | 19.63 |
| ATOM | 481          | CG2 ILE | A | 277 | 4.925  | 39.409 | 30.421 | 1.00 | 21.02 |
| ATOM | 482          | CG1 ILE | A | 277 | 7.212  | 39.101 | 31.390 | 1.00 | 20.19 |
| ATOM | 483          | CD1 ILE | A | 277 | 6.754  | 39.439 | 32.779 | 1.00 | 20.94 |
| ATOM | 484          | C ILE   | A | 277 | 8.385  | 39.741 | 28.763 | 1.00 | 18.46 |
| ATOM | 485          | O ILE   | A | 277 | 9.318  | 39.076 | 29.168 | 1.00 | 16.61 |
| ATOM | 486          | N GLN   | A | 278 | 8.505  | 40.919 | 28.219 | 1.00 | 17.96 |
| ATOM | 487          | CA GLN  | A | 278 | 9.743  | 41.629 | 28.051 | 1.00 | 19.65 |
| ATOM | 488          | CB GLN  | A | 278 | 10.224 | 41.684 | 26.624 | 1.00 | 25.01 |
| ATOM | 489          | CG GLN  | A | 278 | 11.692 | 41.405 | 26.382 | 1.00 | 28.24 |
| ATOM | 490          | CD GLN  | A | 278 | 11.580 | 40.059 | 25.643 | 1.00 | 32.63 |
| ATOM | 491          | OE1 GLN | A | 278 | 11.660 | 40.060 | 24.422 | 1.00 | 33.32 |
| ATOM | 492          | NE2 GLN | A | 278 | 11.331 | 39.078 | 26.502 | 1.00 | 34.14 |
| ATOM | 493          | C GLN   | A | 278 | 9.499  | 43.122 | 28.316 | 1.00 | 17.44 |
| ATOM | 494          | O GLN   | A | 278 | 8.589  | 43.689 | 27.693 | 1.00 | 14.22 |
| ATOM | 495          | N ILE   | A | 279 | 10.537 | 43.709 | 28.900 | 1.00 | 13.53 |
| ATOM | 496          | CA ILE  | A | 279 | 10.471 | 45.146 | 29.090 | 1.00 | 15.82 |
| ATOM | 497          | CB ILE  | A | 279 | 11.441 | 45.658 | 30.183 | 1.00 | 15.54 |
| ATOM | 498          | CG2 ILE | A | 279 | 11.402 | 47.166 | 30.140 | 1.00 | 15.97 |
| ATOM | 499          | CG1 ILE | A | 279 | 11.007 | 45.083 | 31.520 | 1.00 | 16.27 |
| ATOM | 500          | CD1 ILE | A | 279 | 11.940 | 45.388 | 32.661 | 1.00 | 17.52 |
| ATOM | 501          | C ILE   | A | 279 | 10.745 | 45.847 | 27.771 | 1.00 | 16.97 |
| ATOM | 502          | O ILE   | A | 279 | 11.741 | 45.578 | 27.115 | 1.00 | 16.40 |
| ATOM | 503          | N GLU   | A | 280 | 9.824  | 46.719 | 27.370 | 1.00 | 17.63 |
| ATOM | 504          | CA GLU  | A | 280 | 10.019 | 47.523 | 26.185 | 1.00 | 20.86 |
| ATOM | 505          | CB GLU  | A | 280 | 8.744  | 47.778 | 25.395 | 1.00 | 23.07 |
| ATOM | 506          | CG GLU  | A | 280 | 8.890  | 48.784 | 24.268 | 1.00 | 29.11 |
| ATOM | 507          | CD GLU  | A | 280 | 9.843  | 48.327 | 23.189 | 1.00 | 32.61 |
| ATOM | 508          | OE1 GLU | A | 280 | 10.187 | 47.124 | 23.154 | 1.00 | 36.14 |
| ATOM | 509          | OE2 GLU | A | 280 | 10.293 | 49.127 | 22.343 | 1.00 | 34.84 |
| ATOM | 510          | C GLU   | A | 280 | 10.599 | 48.892 | 26.605 | 1.00 | 18.21 |
| ATOM | 511          | O GLU   | A | 280 | 11.426 | 49.511 | 25.941 | 1.00 | 16.53 |
| ATOM | 512          | N GLN   | A | 281 | 10.088 | 49.380 | 27.716 | 1.00 | 18.36 |
| ATOM | 513          | NE2 GLN | A | 281 | 11.497 | 53.112 | 26.056 | 1.00 | 34.24 |
| ATOM | 514          | OE1 GLN | A | 281 | 10.702 | 55.093 | 26.755 | 1.00 | 36.11 |
| ATOM | 515          | CD GLN  | A | 281 | 10.798 | 53.869 | 26.901 | 1.00 | 33.14 |
| ATOM | 516          | CG GLN  | A | 281 | 10.120 | 53.163 | 28.056 | 1.00 | 29.67 |
| ATOM | 517          | CB GLN  | A | 281 | 9.611  | 51.793 | 27.640 | 1.00 | 24.17 |
| ATOM | 518          | CA GLN  | A | 281 | 10.509 | 50.675 | 28.207 | 1.00 | 21.85 |
| ATOM | 519          | C GLN   | A | 281 | 10.385 | 50.730 | 29.723 | 1.00 | 22.08 |
| ATOM | 520          | O GLN   | A | 281 | 9.444  | 50.170 | 30.275 | 1.00 | 19.43 |
| ATOM | 521          | N ILE   | A | 282 | 11.379 | 51.377 | 30.337 | 1.00 | 19.26 |
| ATOM | 522          | CA ILE  | A | 282 | 11.340 | 51.564 | 31.756 | 1.00 | 20.21 |
| ATOM | 523          | CB ILE  | A | 282 | 12.456 | 50.838 | 32.501 | 1.00 | 23.17 |
| ATOM | 524          | CG2 ILE | A | 282 | 12.567 | 51.331 | 33.942 | 1.00 | 22.63 |
| ATOM | 525          | CG1 ILE | A | 282 | 12.183 | 49.337 | 32.486 | 1.00 | 24.53 |
| ATOM | 526          | CD1 ILE | A | 282 | 13.292 | 48.530 | 33.126 | 1.00 | 27.43 |
| ATOM | 527          | C ILE   | A | 282 | 11.408 | 53.062 | 32.033 | 1.00 | 20.13 |

|      | Atom | Type | Residue | ? | #   | X      | Y      | Z      | OCC  | B     |
|------|------|------|---------|---|-----|--------|--------|--------|------|-------|
| ATOM | 528  | O    | ILE     | A | 282 | 12.183 | 53.826 | 31.441 | 1.00 | 21.53 |
| ATOM | 529  | N    | ARG     | A | 283 | 10.595 | 53.478 | 32.972 | 1.00 | 18.99 |
| ATOM | 530  | CA   | ARG     | A | 283 | 10.541 | 54.878 | 33.353 | 1.00 | 20.71 |
| ATOM | 531  | CB   | ARG     | A | 283 | 9.159  | 55.499 | 33.116 | 1.00 | 23.74 |
| ATOM | 532  | CG   | ARG     | A | 283 | 8.779  | 55.516 | 31.645 | 1.00 | 28.61 |
| ATOM | 533  | CD   | ARG     | A | 283 | 9.030  | 56.887 | 31.041 | 1.00 | 33.16 |
| ATOM | 534  | NE   | ARG     | A | 283 | 9.596  | 56.759 | 29.712 | 1.00 | 37.40 |
| ATOM | 535  | CZ   | ARG     | A | 283 | 9.199  | 57.449 | 28.659 | 1.00 | 40.44 |
| ATOM | 536  | NH1  | ARG     | A | 283 | 8.191  | 58.311 | 28.783 | 1.00 | 41.71 |
| ATOM | 537  | NH2  | ARG     | A | 283 | 9.800  | 57.245 | 27.492 | 1.00 | 41.03 |
| ATOM | 538  | C    | ARG     | A | 283 | 10.826 | 54.930 | 34.844 | 1.00 | 20.40 |
| ATOM | 539  | O    | ARG     | A | 283 | 10.049 | 54.339 | 35.566 | 1.00 | 17.37 |
| ATOM | 540  | N    | ILE     | A | 284 | 11.881 | 55.634 | 35.220 | 1.00 | 18.94 |
| ATOM | 541  | CA   | ILE     | A | 284 | 12.127 | 55.779 | 36.655 | 1.00 | 19.58 |
| ATOM | 542  | CB   | ILE     | A | 284 | 13.582 | 55.519 | 37.053 | 1.00 | 20.09 |
| ATOM | 543  | CG2  | ILE     | A | 284 | 13.684 | 55.477 | 38.573 | 1.00 | 20.97 |
| ATOM | 544  | CG1  | ILE     | A | 284 | 14.178 | 54.254 | 36.460 | 1.00 | 20.86 |
| ATOM | 545  | CD1  | ILE     | A | 284 | 13.442 | 52.976 | 36.774 | 1.00 | 20.01 |
| ATOM | 546  | C    | ILE     | A | 284 | 11.792 | 57.228 | 37.002 | 1.00 | 19.71 |
| ATOM | 547  | O    | ILE     | A | 284 | 12.399 | 58.147 | 36.427 | 1.00 | 19.08 |
| ATOM | 548  | N    | LEU     | A | 285 | 10.816 | 57.413 | 37.849 | 1.00 | 19.33 |
| ATOM | 549  | CA   | LEU     | A | 285 | 10.379 | 58.729 | 38.276 | 1.00 | 20.90 |
| ATOM | 550  | CB   | LEU     | A | 285 | 8.881  | 58.729 | 38.557 | 1.00 | 20.57 |
| ATOM | 551  | CG   | LEU     | A | 285 | 8.020  | 58.220 | 37.391 | 1.00 | 18.92 |
| ATOM | 552  | CD1  | LEU     | A | 285 | 6.569  | 58.488 | 37.719 | 1.00 | 19.77 |
| ATOM | 553  | CD2  | LEU     | A | 285 | 8.426  | 58.759 | 36.039 | 1.00 | 18.79 |
| ATOM | 554  | C    | LEU     | A | 285 | 11.153 | 59.078 | 39.542 | 1.00 | 22.65 |
| ATOM | 555  | O    | LEU     | A | 285 | 10.861 | 58.536 | 40.585 | 1.00 | 21.09 |
| ATOM | 556  | N    | LYS     | A | 286 | 12.179 | 59.897 | 39.370 | 1.00 | 23.47 |
| ATOM | 557  | CA   | LYS     | A | 286 | 13.101 | 60.223 | 40.443 | 1.00 | 25.88 |
| ATOM | 558  | CB   | LYS     | A | 286 | 14.400 | 60.777 | 39.830 | 1.00 | 24.64 |
| ATOM | 559  | CG   | LYS     | A | 286 | 15.057 | 59.703 | 38.969 | 1.00 | 26.69 |
| ATOM | 560  | CD   | LYS     | A | 286 | 16.105 | 60.262 | 38.032 | 1.00 | 28.58 |
| ATOM | 561  | CE   | LYS     | A | 286 | 17.308 | 59.334 | 37.986 | 1.00 | 28.89 |
| ATOM | 562  | NZ   | LYS     | A | 286 | 18.328 | 59.807 | 37.012 | 1.00 | 29.92 |
| ATOM | 563  | C    | LYS     | A | 286 | 12.515 | 61.157 | 41.473 | 1.00 | 26.73 |
| ATOM | 564  | O    | LYS     | A | 286 | 12.944 | 61.136 | 42.622 | 1.00 | 28.60 |
| ATOM | 565  | N    | SER     | A | 287 | 11.543 | 61.980 | 41.133 | 1.00 | 25.80 |
| ATOM | 566  | CA   | SER     | A | 287 | 10.969 | 62.865 | 42.158 | 1.00 | 26.18 |
| ATOM | 567  | CB   | SER     | A | 287 | 11.627 | 64.249 | 42.056 | 1.00 | 26.60 |
| ATOM | 568  | OG   | SER     | A | 287 | 11.272 | 64.767 | 40.796 | 1.00 | 28.18 |
| ATOM | 569  | C    | SER     | A | 287 | 9.471  | 62.857 | 41.977 | 1.00 | 24.89 |
| ATOM | 570  | O    | SER     | A | 287 | 8.996  | 62.358 | 40.947 | 1.00 | 25.47 |
| ATOM | 571  | N    | PRO     | A | 288 | 8.739  | 63.268 | 42.989 | 1.00 | 26.04 |
| ATOM | 572  | CD   | PRO     | A | 288 | 9.222  | 63.876 | 44.247 | 1.00 | 27.14 |
| ATOM | 573  | CA   | PRO     | A | 288 | 7.294  | 63.276 | 42.938 | 1.00 | 26.70 |
| ATOM | 574  | CB   | PRO     | A | 288 | 6.831  | 63.561 | 44.339 | 1.00 | 26.05 |
| ATOM | 575  | CG   | PRO     | A | 288 | 8.010  | 63.972 | 45.128 | 1.00 | 27.69 |
| ATOM | 576  | C    | PRO     | A | 288 | 6.826  | 64.313 | 41.928 | 1.00 | 27.00 |
| ATOM | 577  | O    | PRO     | A | 288 | 7.522  | 65.301 | 41.666 | 1.00 | 27.28 |
| ATOM | 578  | N    | GLN     | A | 289 | 5.681  | 64.051 | 41.341 | 1.00 | 25.80 |
| ATOM | 579  | CA   | GLN     | A | 289 | 5.123  | 64.976 | 40.376 | 1.00 | 27.15 |
| ATOM | 580  | CB   | GLN     | A | 289 | 4.021  | 64.214 | 39.628 | 1.00 | 27.78 |
| ATOM | 581  | CG   | GLN     | A | 289 | 3.246  | 65.040 | 38.617 | 1.00 | 27.92 |

|      | Atom |         |   |     |        |        |        |      |       |  |
|------|------|---------|---|-----|--------|--------|--------|------|-------|--|
|      | Type | Residue | Z | #   | X      | Y      | Z      | OCC  | B     |  |
| ATOM | 582  | CD GLN  | A | 289 | 4.207  | 65.636 | 37.616 | 1.00 | 28.41 |  |
| ATOM | 583  | OE1 GLN | A | 289 | 4.970  | 64.944 | 36.966 | 1.00 | 28.03 |  |
| ATOM | 584  | NE2 GLN | A | 289 | 4.179  | 66.966 | 37.505 | 1.00 | 32.04 |  |
| ATOM | 585  | C GLN   | A | 289 | 4.553  | 66.194 | 41.093 | 1.00 | 27.84 |  |
| ATOM | 586  | O GLN   | A | 289 | 3.693  | 66.017 | 41.943 | 1.00 | 27.12 |  |
| ATOM | 587  | N GLU   | A | 290 | 4.962  | 67.414 | 40.766 | 1.00 | 30.72 |  |
| ATOM | 588  | OE2 GLU | A | 290 | 4.477  | 72.113 | 38.486 | 1.00 | 39.70 |  |
| ATOM | 589  | OE1 GLU | A | 290 | 6.067  | 72.564 | 39.857 | 1.00 | 40.48 |  |
| ATOM | 590  | CD GLU  | A | 290 | 5.336  | 71.724 | 39.305 | 1.00 | 39.53 |  |
| ATOM | 591  | CG GLU  | A | 290 | 5.461  | 70.253 | 39.660 | 1.00 | 37.94 |  |
| ATOM | 592  | CB GLU  | A | 290 | 5.094  | 69.910 | 41.084 | 1.00 | 35.71 |  |
| ATOM | 593  | CA GLU  | A | 290 | 4.384  | 68.595 | 41.401 | 1.00 | 33.44 |  |
| ATOM | 594  | C GLU   | A | 290 | 2.912  | 68.679 | 40.978 | 1.00 | 32.66 |  |
| ATOM | 595  | O GLU   | A | 290 | 2.615  | 68.487 | 39.807 | 1.00 | 32.60 |  |
| ATOM | 596  | N VAL   | A | 291 | 2.027  | 68.929 | 41.928 | 1.00 | 32.52 |  |
| ATOM | 597  | CA VAL  | A | 291 | 0.589  | 68.960 | 41.608 | 1.00 | 34.53 |  |
| ATOM | 598  | CB VAL  | A | 291 | 0.016  | 67.667 | 42.214 | 1.00 | 34.68 |  |
| ATOM | 599  | CG1 VAL | A | 291 | -0.992 | 67.828 | 43.317 | 1.00 | 33.99 |  |
| ATOM | 600  | CG2 VAL | A | 291 | -0.509 | 66.742 | 41.114 | 1.00 | 33.97 |  |
| ATOM | 601  | C VAL   | A | 291 | -0.040 | 70.265 | 42.070 | 1.00 | 36.93 |  |
| ATOM | 602  | O VAL   | A | 291 | 0.296  | 70.786 | 43.141 | 1.00 | 35.77 |  |
| ATOM | 603  | N LYS   | A | 292 | -0.879 | 70.860 | 41.231 | 1.00 | 38.91 |  |
| ATOM | 604  | NZ LYS  | A | 292 | 0.250  | 74.239 | 36.361 | 1.00 | 47.09 |  |
| ATOM | 605  | CE LYS  | A | 292 | -0.459 | 74.753 | 37.563 | 1.00 | 45.89 |  |
| ATOM | 606  | CD LYS  | A | 292 | -1.298 | 73.665 | 38.215 | 1.00 | 45.49 |  |
| ATOM | 607  | CG LYS  | A | 292 | -1.226 | 73.759 | 39.722 | 1.00 | 44.08 |  |
| ATOM | 608  | CB LYS  | A | 292 | -2.197 | 72.809 | 40.397 | 1.00 | 42.31 |  |
| ATOM | 609  | CA LYS  | A | 292 | -1.595 | 72.078 | 41.589 | 1.00 | 41.28 |  |
| ATOM | 610  | C LYS   | A | 292 | -2.701 | 71.697 | 42.557 | 1.00 | 41.79 |  |
| ATOM | 611  | O LYS   | A | 292 | -3.085 | 70.535 | 42.624 | 1.00 | 42.72 |  |
| ATOM | 612  | N PRO   | A | 293 | -3.192 | 72.668 | 43.305 | 1.00 | 42.21 |  |
| ATOM | 613  | CD PRO  | A | 293 | -2.802 | 74.096 | 43.247 | 1.00 | 42.59 |  |
| ATOM | 614  | CA PRO  | A | 293 | -4.279 | 72.420 | 44.237 | 1.00 | 41.91 |  |
| ATOM | 615  | CB PRO  | A | 293 | -4.605 | 73.784 | 44.806 | 1.00 | 41.79 |  |
| ATOM | 616  | CG PRO  | A | 293 | -3.481 | 74.676 | 44.450 | 1.00 | 41.90 |  |
| ATOM | 617  | C PRO   | A | 293 | -5.441 | 71.807 | 43.474 | 1.00 | 41.40 |  |
| ATOM | 618  | O PRO   | A | 293 | -5.696 | 72.212 | 42.339 | 1.00 | 41.02 |  |
| ATOM | 619  | N GLY   | A | 294 | -6.059 | 70.755 | 44.003 | 1.00 | 40.85 |  |
| ATOM | 620  | CA GLY  | A | 294 | -7.176 | 70.123 | 43.332 | 1.00 | 41.30 |  |
| ATOM | 621  | C GLY   | A | 294 | -6.832 | 69.033 | 42.332 | 1.00 | 40.98 |  |
| ATOM | 622  | O GLY   | A | 294 | -7.688 | 68.185 | 42.061 | 1.00 | 41.17 |  |
| ATOM | 623  | N GLU   | A | 295 | -5.636 | 69.051 | 41.753 | 1.00 | 39.55 |  |
| ATOM | 624  | OE2 GLU | A | 295 | -2.049 | 69.989 | 38.852 | 1.00 | 44.47 |  |
| ATOM | 625  | OE1 GLU | A | 295 | -3.356 | 71.223 | 37.568 | 1.00 | 44.87 |  |
| ATOM | 626  | CD GLU  | A | 295 | -3.176 | 70.330 | 38.422 | 1.00 | 44.01 |  |
| ATOM | 627  | CG GLU  | A | 295 | -4.422 | 69.647 | 38.946 | 1.00 | 42.26 |  |
| ATOM | 628  | CB GLU  | A | 295 | -4.099 | 68.521 | 39.886 | 1.00 | 39.91 |  |
| ATOM | 629  | CA GLU  | A | 295 | -5.214 | 68.044 | 40.813 | 1.00 | 38.60 |  |
| ATOM | 630  | C GLU   | A | 295 | -4.641 | 66.825 | 41.552 | 1.00 | 36.59 |  |
| ATOM | 631  | O GLU   | A | 295 | -4.281 | 66.871 | 42.720 | 1.00 | 36.85 |  |
| ATOM | 632  | N LYS   | A | 296 | -4.418 | 65.777 | 40.773 | 1.00 | 33.95 |  |
| ATOM | 633  | CA LYS  | A | 296 | -3.782 | 64.575 | 41.294 | 1.00 | 30.68 |  |
| ATOM | 634  | CB LYS  | A | 296 | -4.755 | 63.656 | 41.996 | 1.00 | 31.56 |  |
| ATOM | 635  | CG LYS  | A | 296 | -5.992 | 63.312 | 41.185 | 1.00 | 32.22 |  |



| Atom |     | Type | Residue | Z | #   | X      | Y      | Z      | OCC  | B     |
|------|-----|------|---------|---|-----|--------|--------|--------|------|-------|
| ATOM | 636 | CD   | LYS     | A | 296 | -7.149 | 62.924 | 42.075 | 1.00 | 32.13 |
| ATOM | 637 | CE   | LYS     | A | 296 | -8.161 | 62.034 | 41.381 | 1.00 | 33.43 |
| ATOM | 638 | NZ   | LYS     | A | 296 | -8.106 | 62.091 | 39.904 | 1.00 | 34.90 |
| ATOM | 639 | C    | LYS     | A | 296 | -3.028 | 63.883 | 40.167 | 1.00 | 28.79 |
| ATOM | 640 | O    | LYS     | A | 296 | -3.275 | 64.112 | 38.986 | 1.00 | 27.50 |
| ATOM | 641 | N    | HIS     | A | 297 | -1.999 | 63.135 | 40.580 | 1.00 | 25.20 |
| ATOM | 642 | CA   | HIS     | A | 297 | -1.216 | 62.396 | 39.584 | 1.00 | 20.71 |
| ATOM | 643 | CB   | HIS     | A | 297 | -0.148 | 63.267 | 38.981 | 1.00 | 20.06 |
| ATOM | 644 | CG   | HIS     | A | 297 | 0.824  | 62.612 | 38.054 | 1.00 | 18.56 |
| ATOM | 645 | CD2  | HIS     | A | 297 | 1.808  | 61.741 | 38.309 | 1.00 | 15.40 |
| ATOM | 646 | ND1  | HIS     | A | 297 | 0.863  | 62.878 | 36.701 | 1.00 | 18.13 |
| ATOM | 647 | CE1  | HIS     | A | 297 | 1.844  | 62.180 | 36.160 | 1.00 | 17.97 |
| ATOM | 648 | NE2  | HIS     | A | 297 | 2.416  | 61.463 | 37.105 | 1.00 | 19.72 |
| ATOM | 649 | C    | HIS     | A | 297 | -0.730 | 61.151 | 40.292 | 1.00 | 19.15 |
| ATOM | 650 | O    | HIS     | A | 297 | -0.477 | 61.256 | 41.493 | 1.00 | 18.54 |
| ATOM | 651 | N    | TYR     | A | 298 | -0.557 | 60.030 | 39.580 | 1.00 | 18.21 |
| ATOM | 652 | CA   | TYR     | A | 298 | -0.155 | 58.824 | 40.330 | 1.00 | 16.80 |
| ATOM | 653 | CB   | TYR     | A | 298 | -0.193 | 57.594 | 39.437 | 1.00 | 16.24 |
| ATOM | 654 | CG   | TYR     | A | 298 | 0.940  | 57.509 | 38.444 | 1.00 | 17.23 |
| ATOM | 655 | CD1  | TYR     | A | 298 | 2.077  | 56.755 | 38.742 | 1.00 | 15.56 |
| ATOM | 656 | CE1  | TYR     | A | 298 | 3.094  | 56.667 | 37.821 | 1.00 | 15.21 |
| ATOM | 657 | CD2  | TYR     | A | 298 | 0.881  | 58.184 | 37.236 | 1.00 | 16.74 |
| ATOM | 658 | CE2  | TYR     | A | 298 | 1.913  | 58.098 | 36.337 | 1.00 | 16.91 |
| ATOM | 659 | CZ   | TYR     | A | 298 | 3.022  | 57.325 | 36.636 | 1.00 | 16.49 |
| ATOM | 660 | OH   | TYR     | A | 298 | 4.046  | 57.260 | 35.719 | 1.00 | 18.10 |
| ATOM | 661 | C    | TYR     | A | 298 | 1.185  | 58.981 | 41.029 | 1.00 | 16.63 |
| ATOM | 662 | O    | TYR     | A | 298 | 1.351  | 58.330 | 42.073 | 1.00 | 16.70 |
| ATOM | 663 | N    | ASN     | A | 299 | 2.112  | 59.766 | 40.523 | 1.00 | 16.99 |
| ATOM | 664 | CA   | ASN     | A | 299 | 3.423  | 60.011 | 41.085 | 1.00 | 18.59 |
| ATOM | 665 | CB   | ASN     | A | 299 | 4.463  | 60.166 | 39.965 | 1.00 | 18.92 |
| ATOM | 666 | CG   | ASN     | A | 299 | 5.890  | 60.214 | 40.494 | 1.00 | 18.76 |
| ATOM | 667 | OD1  | ASN     | A | 299 | 6.205  | 59.456 | 41.412 | 1.00 | 18.23 |
| ATOM | 668 | ND2  | ASN     | A | 299 | 6.748  | 61.070 | 39.950 | 1.00 | 19.19 |
| ATOM | 669 | C    | ASN     | A | 299 | 3.513  | 61.224 | 42.009 | 1.00 | 20.06 |
| ATOM | 670 | O    | ASN     | A | 299 | 4.606  | 61.723 | 42.362 | 1.00 | 18.80 |
| ATOM | 671 | N    | MET     | A | 300 | 2.395  | 61.732 | 42.509 | 1.00 | 20.80 |
| ATOM | 672 | CA   | MET     | A | 300 | 2.449  | 62.886 | 43.417 | 1.00 | 22.77 |
| ATOM | 673 | CB   | MET     | A | 300 | 1.115  | 63.568 | 43.608 | 1.00 | 23.16 |
| ATOM | 674 | CG   | MET     | A | 300 | 0.029  | 62.931 | 44.436 | 1.00 | 25.10 |
| ATOM | 675 | SD   | MET     | A | 300 | -1.590 | 63.723 | 44.020 | 1.00 | 28.00 |
| ATOM | 676 | CE   | MET     | A | 300 | -2.640 | 62.839 | 45.144 | 1.00 | 24.04 |
| ATOM | 677 | C    | MET     | A | 300 | 3.012  | 62.458 | 44.767 | 1.00 | 21.89 |
| ATOM | 678 | O    | MET     | A | 300 | 2.833  | 61.314 | 45.160 | 1.00 | 18.53 |
| ATOM | 679 | N    | ALA     | A | 301 | 3.369  | 63.413 | 45.606 | 1.00 | 22.83 |
| ATOM | 680 | CA   | ALA     | A | 301 | 3.872  | 63.134 | 46.926 | 1.00 | 23.87 |
| ATOM | 681 | CB   | ALA     | A | 301 | 4.450  | 64.429 | 47.484 | 1.00 | 23.72 |
| ATOM | 682 | C    | ALA     | A | 301 | 2.841  | 62.580 | 47.893 | 1.00 | 24.63 |
| ATOM | 683 | O    | ALA     | A | 301 | 3.085  | 61.615 | 48.637 | 1.00 | 23.46 |
| ATOM | 684 | N    | LYS     | A | 302 | 1.652  | 63.178 | 47.913 | 1.00 | 26.09 |
| ATOM | 685 | CA   | LYS     | A | 302 | 0.645  | 62.719 | 48.859 | 1.00 | 26.00 |
| ATOM | 686 | CB   | LYS     | A | 302 | -0.215 | 63.890 | 49.329 | 1.00 | 28.38 |
| ATOM | 687 | CG   | LYS     | A | 302 | 0.554  | 65.188 | 49.528 | 1.00 | 29.29 |
| ATOM | 688 | CD   | LYS     | A | 302 | 1.697  | 65.125 | 50.505 | 1.00 | 30.98 |
| ATOM | 689 | CE   | LYS     | A | 302 | 2.522  | 66.407 | 50.512 | 1.00 | 32.65 |

|      | Atom | Type | Residue | Z | #   | X       | Y      | Z      | OCC    | B     |
|------|------|------|---------|---|-----|---------|--------|--------|--------|-------|
| ATOM | 690  | NZ   | LYS     | A | 302 | 2.617   | 67.085 | 49.191 | 1.00   | 33.62 |
| ATOM | 691  | C    | LYS     | A | 302 | -0.198  | 61.580 | 48.291 | 1.00   | 25.55 |
| ATOM | 692  | O    | LYS     | A | 302 | -0.295  | 61.399 | 47.087 | 1.00   | 24.72 |
| ATOM | 693  | N    | SER     | A | 303 | -0.793  | 60.835 | 49.202 | 1.00   | 24.45 |
| ATOM | 694  | CA   | SER     | A | 303 | -1.621  | 59.696 | 48.836 | 1.00   | 25.50 |
| ATOM | 695  | CB   | SER     | A | 303 | -1.434  | 58.619 | 49.878 | 1.00   | 26.64 |
| ATOM | 696  | OG   | SER     | A | 303 | -1.869  | 59.030 | 51.149 | 1.00   | 31.03 |
| ATOM | 697  | C    | SER     | A | 303 | -3.052  | 60.182 | 48.666 | 1.00   | 25.87 |
| ATOM | 698  | O    | SER     | A | 303 | -3.396  | 61.256 | 49.185 | 1.00   | 22.73 |
| ATOM | 699  | N    | TYR     | A | 304 | -3.814  | 59.454 | 47.855 | 1.00   | 24.98 |
| ATOM | 700  | CA   | TYR     | A | 304 | -5.181  | 59.862 | 47.550 | 1.00   | 24.27 |
| ATOM | 701  | CB   | TYR     | A | 304 | -5.140  | 60.449 | 46.132 | 1.00   | 25.45 |
| ATOM | 702  | CG   | TYR     | A | 304 | -6.466  | 61.015 | 45.686 | 1.00   | 28.35 |
| ATOM | 703  | CD1  | TYR     | A | 304 | -6.762  | 62.357 | 45.929 | 1.00   | 29.08 |
| ATOM | 704  | CE1  | TYR     | A | 304 | -7.978  | 62.891 | 45.552 | 1.00   | 29.59 |
| ATOM | 705  | CD2  | TYR     | A | 304 | -7.426  | 60.214 | 45.085 | 1.00   | 27.54 |
| ATOM | 706  | CE2  | TYR     | A | 304 | -8.630  | 60.754 | 44.702 | 1.00   | 29.33 |
| ATOM | 707  | CZ   | TYR     | A | 304 | -8.893  | 62.094 | 44.944 | 1.00   | 29.27 |
| ATOM | 708  | OH   | TYR     | A | 304 | -10.103 | 62.610 | 44.578 | 1.00   | 32.08 |
| ATOM | 709  | C    | TYR     | A | 304 | -6.192  | 58.769 | 47.721 | 1.00   | 25.14 |
| ATOM | 710  | O    | TYR     | A | 304 | -5.707  | 57.735 | 47.336 | 1.0000 | 20.08 |
| ATOM | 711  | N    | PRO     | A | 305 | -7.356  | 59.000 | 48.279 | 1.00   | 26.60 |
| ATOM | 712  | CD   | PRO     | A | 305 | -8.386  | 58.001 | 48.459 | 1.00   | 25.22 |
| ATOM | 713  | CA   | PRO     | A | 305 | -7.989  | 60.240 | 48.637 | 1.00   | 27.02 |
| ATOM | 714  | CB   | PRO     | A | 305 | -9.492  | 60.083 | 48.491 | 1.00   | 25.75 |
| ATOM | 715  | CG   | PRO     | A | 305 | -9.707  | 58.646 | 48.789 | 1.00   | 25.74 |
| ATOM | 716  | C    | PRO     | A | 305 | -7.625  | 60.782 | 50.007 | 1.00   | 28.63 |
| ATOM | 717  | O    | PRO     | A | 305 | -7.922  | 61.915 | 50.430 | 1.00   | 28.68 |
| ATOM | 718  | N    | ASN     | A | 306 | -6.988  | 59.904 | 50.783 | 1.00   | 29.14 |
| ATOM | 719  | CA   | ASN     | A | 306 | -6.713  | 60.273 | 52.173 | 1.00   | 30.26 |
| ATOM | 720  | CB   | ASN     | A | 306 | -7.350  | 59.232 | 53.075 | 1.00   | 32.58 |
| ATOM | 721  | CG   | ASN     | A | 306 | -8.766  | 58.861 | 52.676 | 1.00   | 35.48 |
| ATOM | 722  | OD1  | ASN     | A | 306 | -9.661  | 59.712 | 52.612 | 1.00   | 36.24 |
| ATOM | 723  | ND2  | ASN     | A | 306 | -8.992  | 57.588 | 52.368 | 1.00   | 36.01 |
| ATOM | 724  | C    | ASN     | A | 306 | -5.229  | 60.477 | 52.375 | 1.00   | 29.94 |
| ATOM | 725  | O    | ASN     | A | 306 | -4.444  | 59.536 | 52.439 | 1.00   | 28.29 |
| ATOM | 726  | N    | GLU     | A | 307 | -4.819  | 61.724 | 52.507 | 1.00   | 29.94 |
| ATOM | 727  | OE2  | GLU     | A | 307 | -2.295  | 66.669 | 51.130 | 1.00   | 41.44 |
| ATOM | 728  | OE1  | GLU     | A | 307 | -2.711  | 66.223 | 53.238 | 1.00   | 41.35 |
| ATOM | 729  | CD   | GLU     | A | 307 | -2.656  | 65.896 | 52.037 | 1.00   | 40.02 |
| ATOM | 730  | CG   | GLU     | A | 307 | -3.034  | 64.464 | 51.678 | 1.00   | 38.20 |
| ATOM | 731  | CB   | GLU     | A | 307 | -3.401  | 63.683 | 52.914 | 1.00   | 33.77 |
| ATOM | 732  | CA   | GLU     | A | 307 | -3.461  | 62.152 | 52.717 | 1.00   | 32.32 |
| ATOM | 733  | C    | GLU     | A | 307 | -2.770  | 61.594 | 53.949 | 1.00   | 30.24 |
| ATOM | 734  | O    | GLU     | A | 307 | -1.542  | 61.522 | 53.970 | 1.00   | 30.44 |
| ATOM | 735  | N    | GLU     | A | 308 | -3.513  | 61.273 | 54.984 | 1.00   | 29.39 |
| ATOM | 736  | OE2  | GLU     | A | 308 | -6.099  | 61.320 | 55.501 | 1.00   | 38.47 |
| ATOM | 737  | OE1  | GLU     | A | 308 | -7.129  | 59.531 | 56.089 | 1.00   | 37.95 |
| ATOM | 738  | CD   | GLU     | A | 308 | -6.176  | 60.330 | 56.250 | 1.00   | 36.70 |
| ATOM | 739  | CG   | GLU     | A | 308 | -5.168  | 60.057 | 57.322 | 1.00   | 35.39 |
| ATOM | 740  | CB   | GLU     | A | 308 | -3.931  | 60.913 | 57.384 | 1.00   | 33.10 |
| ATOM | 741  | CA   | GLU     | A | 308 | -2.950  | 60.795 | 56.224 | 1.00   | 29.98 |
| ATOM | 742  | C    | GLU     | A | 308 | -2.487  | 59.353 | 56.093 | 1.00   | 28.21 |
| ATOM | 743  | O    | GLU     | A | 308 | -1.607  | 58.963 | 56.857 | 1.00   | 26.31 |

|      | <u>Atom</u> | <u>Type</u> | <u>Residue</u> | <u>?</u> | <u>#</u> | <u>X</u> | <u>Y</u> | <u>Z</u> | <u>OCC</u> | <u>B</u> |
|------|-------------|-------------|----------------|----------|----------|----------|----------|----------|------------|----------|
| ATOM | 744         | N           | LYS            | A        | 309      | -3.004   | 58.626   | 55.094   | 1.00       | 24.19    |
| ATOM | 745         | CA          | LYS            | A        | 309      | -2.648   | 57.216   | 55.015   | 1.00       | 24.20    |
| ATOM | 746         | CB          | LYS            | A        | 309      | -3.711   | 56.413   | 54.263   | 1.00       | 24.89    |
| ATOM | 747         | CG          | LYS            | A        | 309      | -5.098   | 56.344   | 54.884   | 1.00       | 27.73    |
| ATOM | 748         | CD          | LYS            | A        | 309      | -5.089   | 56.571   | 56.361   | 1.00       | 31.22    |
| ATOM | 749         | CE          | LYS            | A        | 309      | -6.317   | 56.792   | 57.162   | 1.00       | 32.52    |
| ATOM | 750         | NZ          | LYS            | A        | 309      | -6.638   | 55.694   | 58.107   | 1.00       | 34.53    |
| ATOM | 751         | C           | LYS            | A        | 309      | -1.285   | 57.012   | 54.387   | 1.00       | 21.98    |
| ATOM | 752         | O           | LYS            | A        | 309      | -0.832   | 57.851   | 53.636   | 1.00       | 22.27    |
| ATOM | 753         | N           | ASP            | A        | 310      | -0.675   | 55.855   | 54.593   | 1.00       | 20.75    |
| ATOM | 754         | CA          | ASP            | A        | 310      | 0.605    | 55.530   | 53.953   | 1.00       | 20.70    |
| ATOM | 755         | CB          | ASP            | A        | 310      | 1.130    | 54.173   | 54.501   | 1.00       | 20.19    |
| ATOM | 756         | CG          | ASP            | A        | 310      | 2.615    | 54.085   | 54.167   | 1.00       | 22.21    |
| ATOM | 757         | OD1         | ASP            | A        | 310      | 3.335    | 54.893   | 54.831   | 1.00       | 24.55    |
| ATOM | 758         | OD2         | ASP            | A        | 310      | 3.040    | 53.306   | 53.292   | 1.00       | 18.20    |
| ATOM | 759         | C           | ASP            | A        | 310      | 0.474    | 55.419   | 52.450   | 1.00       | 19.43    |
| ATOM | 760         | O           | ASP            | A        | 310      | 1.385    | 55.706   | 51.651   | 1.00       | 20.19    |
| ATOM | 761         | N           | ALA            | A        | 311      | -0.727   | 55.044   | 51.990   | 1.00       | 18.69    |
| ATOM | 762         | CA          | ALA            | A        | 311      | -0.947   | 54.834   | 50.572   | 1.00       | 17.44    |
| ATOM | 763         | CB          | ALA            | A        | 311      | -0.991   | 53.296   | 50.429   | 1.00       | 16.55    |
| ATOM | 764         | C           | ALA            | A        | 311      | -2.302   | 55.316   | 50.028   | 1.00       | 16.60    |
| ATOM | 765         | O           | ALA            | A        | 311      | -3.221   | 55.655   | 50.751   | 1.00       | 12.08    |
| ATOM | 766         | N           | TRP            | A        | 312      | -2.339   | 55.302   | 48.711   | 1.00       | 17.19    |
| ATOM | 767         | CA          | TRP            | A        | 312      | -3.555   | 55.615   | 47.963   | 1.00       | 15.85    |
| ATOM | 768         | CB          | TRP            | A        | 312      | -3.236   | 55.569   | 46.483   | 1.00       | 14.37    |
| ATOM | 769         | CG          | TRP            | A        | 312      | -2.713   | 56.757   | 45.760   | 1.00       | 16.10    |
| ATOM | 770         | CD2         | TRP            | A        | 312      | -3.413   | 57.526   | 44.772   | 1.00       | 16.24    |
| ATOM | 771         | CE2         | TRP            | A        | 312      | -2.554   | 58.554   | 44.342   | 1.00       | 17.46    |
| ATOM | 772         | CE3         | TRP            | A        | 312      | -4.685   | 57.427   | 44.204   | 1.00       | 17.59    |
| ATOM | 773         | CD1         | TRP            | A        | 312      | -1.492   | 57.360   | 45.884   | 1.00       | 15.52    |
| ATOM | 774         | NE1         | TRP            | A        | 312      | -1.381   | 58.440   | 45.050   | 1.00       | 16.75    |
| ATOM | 775         | CZ2         | TRP            | A        | 312      | -2.900   | 59.475   | 43.357   | 1.00       | 17.80    |
| ATOM | 776         | CZ3         | TRP            | A        | 312      | -5.022   | 58.348   | 43.228   | 1.00       | 15.80    |
| ATOM | 777         | CH2         | TRP            | A        | 312      | -4.154   | 59.345   | 42.828   | 1.00       | 17.23    |
| ATOM | 778         | C           | TRP            | A        | 312      | -4.562   | 54.502   | 48.204   | 1.00       | 16.18    |
| ATOM | 779         | O           | TRP            | A        | 312      | -4.185   | 53.393   | 48.559   | 1.00       | 14.62    |
| ATOM | 780         | N           | ASP            | A        | 313      | -5.841   | 54.750   | 47.906   | 1.00       | 17.14    |
| ATOM | 781         | CA          | ASP            | A        | 313      | -6.817   | 53.682   | 47.741   | 1.00       | 17.42    |
| ATOM | 782         | CB          | ASP            | A        | 313      | -8.170   | 54.298   | 47.343   | 1.00       | 19.70    |
| ATOM | 783         | CG          | ASP            | A        | 313      | -9.106   | 53.244   | 46.797   | 1.00       | 22.89    |
| ATOM | 784         | OD1         | ASP            | A        | 313      | -9.073   | 52.935   | 45.598   | 1.00       | 24.60    |
| ATOM | 785         | OD2         | ASP            | A        | 313      | -9.841   | 52.697   | 47.623   | 1.00       | 26.78    |
| ATOM | 786         | C           | ASP            | A        | 313      | -6.273   | 52.903   | 46.539   | 1.00       | 14.58    |
| ATOM | 787         | O           | ASP            | A        | 313      | -6.033   | 53.570   | 45.533   | 1.00       | 14.85    |
| ATOM | 788         | N           | VAL            | A        | 314      | -6.101   | 51.596   | 46.588   | 1.00       | 15.33    |
| ATOM | 789         | CA          | VAL            | A        | 314      | -5.434   | 50.915   | 45.475   | 1.00       | 14.25    |
| ATOM | 790         | CB          | VAL            | A        | 314      | -5.067   | 49.478   | 45.891   | 1.00       | 13.94    |
| ATOM | 791         | CG1         | VAL            | A        | 314      | -6.266   | 48.578   | 46.107   | 1.00       | 12.58    |
| ATOM | 792         | CG2         | VAL            | A        | 314      | -4.090   | 48.891   | 44.864   | 1.00       | 12.94    |
| ATOM | 793         | C           | VAL            | A        | 314      | -6.110   | 50.966   | 44.129   | 1.00       | 14.22    |
| ATOM | 794         | O           | VAL            | A        | 314      | -5.480   | 51.152   | 43.099   | 1.00       | 13.01    |
| ATOM | 795         | N           | LYS            | A        | 315      | -7.435   | 50.819   | 44.092   | 1.00       | 16.35    |
| ATOM | 796         | NZ          | LYS            | A        | 315      | -12.342  | 48.884   | 46.668   | 1.00       | 27.78    |
| ATOM | 797         | CE          | LYS            | A        | 315      | -11.908  | 48.279   | 45.365   | 1.00       | 26.99    |

|      | Atom | Type | Residue | Z | #   | X       | Y      | Z      | OCC  | B     |
|------|------|------|---------|---|-----|---------|--------|--------|------|-------|
| ATOM | 798  | CD   | LYS     | A | 315 | -11.499 | 49.287 | 44.334 | 1.00 | 24.72 |
| ATOM | 799  | CG   | LYS     | A | 315 | -10.084 | 49.278 | 43.775 | 1.00 | 21.52 |
| ATOM | 800  | CB   | LYS     | A | 315 | -9.700  | 50.621 | 43.204 | 1.00 | 18.30 |
| ATOM | 801  | CA   | LYS     | A | 315 | -8.223  | 50.882 | 42.870 | 1.00 | 17.01 |
| ATOM | 802  | C    | LYS     | A | 315 | -8.111  | 52.273 | 42.255 | 1.00 | 15.42 |
| ATOM | 803  | O    | LYS     | A | 315 | -7.967  | 52.432 | 41.065 | 1.00 | 14.82 |
| ATOM | 804  | N    | MET     | A | 316 | -8.189  | 53.317 | 43.095 | 1.00 | 16.67 |
| ATOM | 805  | CA   | MET     | A | 316 | -8.023  | 54.673 | 42.531 | 1.00 | 16.96 |
| ATOM | 806  | CB   | MET     | A | 316 | -8.395  | 55.717 | 43.579 | 1.00 | 19.66 |
| ATOM | 807  | CG   | MET     | A | 316 | -9.874  | 55.616 | 43.966 | 1.00 | 21.49 |
| ATOM | 808  | SD   | MET     | A | 316 | -10.303 | 56.858 | 45.216 | 1.00 | 25.95 |
| ATOM | 809  | CE   | MET     | A | 316 | -11.921 | 56.212 | 45.655 | 1.00 | 23.70 |
| ATOM | 810  | C    | MET     | A | 316 | -6.624  | 54.927 | 41.996 | 1.00 | 16.13 |
| ATOM | 811  | O    | MET     | A | 316 | -6.463  | 55.672 | 41.038 | 1.00 | 16.38 |
| ATOM | 812  | N    | LEU     | A | 317 | -5.583  | 54.315 | 42.552 | 1.00 | 15.29 |
| ATOM | 813  | CA   | LEU     | A | 317 | -4.218  | 54.490 | 42.078 | 1.00 | 13.26 |
| ATOM | 814  | CB   | LEU     | A | 317 | -3.200  | 53.915 | 43.097 | 1.00 | 11.74 |
| ATOM | 815  | CG   | LEU     | A | 317 | -1.733  | 54.036 | 42.672 | 1.00 | 12.04 |
| ATOM | 816  | CD1  | LEU     | A | 317 | -1.323  | 55.505 | 42.512 | 1.00 | 10.99 |
| ATOM | 817  | CD2  | LEU     | A | 317 | -0.861  | 53.326 | 43.698 | 1.00 | 11.54 |
| ATOM | 818  | C    | LEU     | A | 317 | -4.079  | 53.785 | 40.755 | 1.00 | 12.38 |
| ATOM | 819  | O    | LEU     | A | 317 | -3.526  | 54.334 | 39.819 | 1.00 | 14.48 |
| ATOM | 820  | N    | LEU     | A | 318 | -4.637  | 52.580 | 40.616 | 1.00 | 12.87 |
| ATOM | 821  | CA   | LEU     | A | 318 | -4.561  | 51.890 | 39.326 | 1.00 | 12.84 |
| ATOM | 822  | CB   | LEU     | A | 318 | -5.112  | 50.457 | 39.453 | 1.00 | 12.79 |
| ATOM | 823  | CG   | LEU     | A | 318 | -4.966  | 49.629 | 38.170 | 1.00 | 14.82 |
| ATOM | 824  | CD1  | LEU     | A | 318 | -3.531  | 49.542 | 37.700 | 1.00 | 15.86 |
| ATOM | 825  | CD2  | LEU     | A | 318 | -5.558  | 48.241 | 38.355 | 1.00 | 14.73 |
| ATOM | 826  | C    | LEU     | A | 318 | -5.230  | 52.673 | 38.218 | 1.00 | 12.07 |
| ATOM | 827  | O    | LEU     | A | 318 | -4.780  | 52.829 | 37.099 | 1.00 | 12.74 |
| ATOM | 828  | N    | GLU     | A | 319 | -6.420  | 53.193 | 38.511 | 1.00 | 15.24 |
| ATOM | 829  | OE2  | GLU     | A | 319 | -11.483 | 52.210 | 39.220 | 1.00 | 28.26 |
| ATOM | 830  | OE1  | GLU     | A | 319 | -10.797 | 54.093 | 40.042 | 1.00 | 29.42 |
| ATOM | 831  | CD   | GLU     | A | 319 | -10.674 | 53.181 | 39.193 | 1.00 | 27.45 |
| ATOM | 832  | CG   | GLU     | A | 319 | -9.561  | 53.233 | 38.177 | 1.00 | 24.55 |
| ATOM | 833  | CB   | GLU     | A | 319 | -8.553  | 54.375 | 38.270 | 1.00 | 18.18 |
| ATOM | 834  | CA   | GLU     | A | 319 | -7.199  | 54.025 | 37.614 | 1.00 | 15.25 |
| ATOM | 835  | C    | GLU     | A | 319 | -6.421  | 55.288 | 37.289 | 1.00 | 14.06 |
| ATOM | 836  | O    | GLU     | A | 319 | -6.317  | 55.697 | 36.141 | 1.00 | 13.57 |
| ATOM | 837  | N    | GLN     | A | 320 | -5.879  | 55.947 | 38.303 | 1.00 | 14.48 |
| ATOM | 838  | CA   | GLN     | A | 320 | -5.086  | 57.164 | 38.073 | 1.00 | 15.95 |
| ATOM | 839  | CB   | GLN     | A | 320 | -4.631  | 57.772 | 39.413 | 1.00 | 17.37 |
| ATOM | 840  | CG   | GLN     | A | 320 | -3.969  | 59.147 | 39.262 | 1.00 | 20.30 |
| ATOM | 841  | CD   | GLN     | A | 320 | -4.917  | 60.189 | 38.681 | 1.00 | 20.82 |
| ATOM | 842  | OE1  | GLN     | A | 320 | -6.069  | 60.198 | 39.101 | 1.00 | 22.55 |
| ATOM | 843  | NE2  | GLN     | A | 320 | -4.480  | 61.016 | 37.768 | 1.00 | 20.50 |
| ATOM | 844  | C    | GLN     | A | 320 | -3.896  | 56.849 | 37.206 | 1.00 | 15.14 |
| ATOM | 845  | O    | GLN     | A | 320 | -3.545  | 57.572 | 36.274 | 1.00 | 16.35 |
| ATOM | 846  | N    | PHE     | A | 321 | -3.178  | 55.751 | 37.535 | 1.00 | 14.19 |
| ATOM | 847  | CA   | PHE     | A | 321 | -1.997  | 55.416 | 36.728 | 1.00 | 13.62 |
| ATOM | 848  | CB   | PHE     | A | 321 | -1.389  | 54.100 | 37.277 | 1.00 | 14.84 |
| ATOM | 849  | CG   | PHE     | A | 321 | -0.286  | 53.531 | 36.462 | 1.00 | 14.25 |
| ATOM | 850  | CD1  | PHE     | A | 321 | 0.874   | 54.232 | 36.256 | 1.00 | 16.53 |
| ATOM | 851  | CD2  | PHE     | A | 321 | -0.407  | 52.275 | 35.889 | 1.00 | 15.71 |

|      | Atom | Type | Residue | ? | #   | X      | Y      | Z      | OCC  | B     |
|------|------|------|---------|---|-----|--------|--------|--------|------|-------|
| ATOM | 852  | CE1  | PHE     | A | 321 | 1.915  | 53.714 | 35.499 | 1.00 | 16.96 |
| ATOM | 853  | CE2  | PHE     | A | 321 | 0.594  | 51.737 | 35.109 | 1.00 | 16.98 |
| ATOM | 854  | CZ   | PHE     | A | 321 | 1.760  | 52.464 | 34.920 | 1.00 | 19.64 |
| ATOM | 855  | C    | PHE     | A | 321 | -2.367 | 55.265 | 35.284 | 1.00 | 15.37 |
| ATOM | 856  | O    | PHE     | A | 321 | -1.743 | 55.838 | 34.391 | 1.00 | 17.95 |
| ATOM | 857  | N    | SER     | A | 322 | -3.440 | 54.502 | 35.011 | 1.00 | 15.65 |
| ATOM | 858  | CA   | SER     | A | 322 | -3.862 | 54.261 | 33.650 | 1.00 | 16.47 |
| ATOM | 859  | CB   | SER     | A | 322 | -5.052 | 53.312 | 33.545 | 1.00 | 17.62 |
| ATOM | 860  | OG   | SER     | A | 322 | -4.956 | 52.111 | 34.281 | 1.00 | 21.90 |
| ATOM | 861  | C    | SER     | A | 322 | -4.219 | 55.608 | 32.980 | 1.00 | 15.02 |
| ATOM | 862  | O    | SER     | A | 322 | -3.836 | 55.773 | 31.839 | 1.00 | 15.73 |
| ATOM | 863  | N    | PHE     | A | 323 | -4.855 | 56.499 | 33.694 | 1.00 | 15.76 |
| ATOM | 864  | CA   | PHE     | A | 323 | -5.163 | 57.831 | 33.153 | 1.00 | 17.15 |
| ATOM | 865  | CB   | PHE     | A | 323 | -5.953 | 58.697 | 34.136 | 1.00 | 18.22 |
| ATOM | 866  | CG   | PHE     | A | 323 | -6.374 | 60.050 | 33.604 | 1.00 | 20.68 |
| ATOM | 867  | CD1  | PHE     | A | 323 | -5.660 | 61.195 | 33.861 | 1.00 | 21.45 |
| ATOM | 868  | CD2  | PHE     | A | 323 | -7.524 | 60.161 | 32.852 | 1.00 | 22.31 |
| ATOM | 869  | CE1  | PHE     | A | 323 | -6.032 | 62.425 | 33.329 | 1.00 | 22.60 |
| ATOM | 870  | CE2  | PHE     | A | 323 | -7.945 | 61.384 | 32.325 | 1.00 | 24.15 |
| ATOM | 871  | CZ   | PHE     | A | 323 | -7.175 | 62.502 | 32.558 | 1.00 | 23.26 |
| ATOM | 872  | C    | PHE     | A | 323 | -3.897 | 58.570 | 32.756 | 1.00 | 18.08 |
| ATOM | 873  | O    | PHE     | A | 323 | -3.807 | 59.053 | 31.648 | 1.00 | 15.95 |
| ATOM | 874  | N    | ASP     | A | 324 | -2.913 | 58.698 | 33.662 | 1.00 | 19.20 |
| ATOM | 875  | CA   | ASP     | A | 324 | -1.748 | 59.521 | 33.405 | 1.00 | 20.57 |
| ATOM | 876  | CB   | ASP     | A | 324 | -0.994 | 59.740 | 34.742 | 1.00 | 23.05 |
| ATOM | 877  | CG   | ASP     | A | 324 | -1.773 | 60.624 | 35.687 | 1.00 | 23.08 |
| ATOM | 878  | OD1  | ASP     | A | 324 | -1.894 | 60.419 | 36.896 | 1.00 | 22.69 |
| ATOM | 879  | OD2  | ASP     | A | 324 | -2.335 | 61.620 | 35.188 | 1.00 | 26.34 |
| ATOM | 880  | C    | ASP     | A | 324 | -0.746 | 58.999 | 32.402 | 1.00 | 21.82 |
| ATOM | 881  | O    | ASP     | A | 324 | -0.058 | 59.793 | 31.764 | 1.00 | 21.73 |
| ATOM | 882  | N    | ILE     | A | 325 | -0.672 | 57.679 | 32.240 | 1.00 | 21.33 |
| ATOM | 883  | CA   | ILE     | A | 325 | 0.264  | 57.038 | 31.339 | 1.00 | 22.61 |
| ATOM | 884  | CB   | ILE     | A | 325 | 0.922  | 55.889 | 32.161 | 1.00 | 25.69 |
| ATOM | 885  | CG2  | ILE     | A | 325 | 0.154  | 54.579 | 32.043 | 1.00 | 24.65 |
| ATOM | 886  | CG1  | ILE     | A | 325 | 2.370  | 55.730 | 31.765 | 1.00 | 26.90 |
| ATOM | 887  | CD1  | ILE     | A | 325 | 3.369  | 56.465 | 32.631 | 1.00 | 27.55 |
| ATOM | 888  | C    | ILE     | A | 325 | -0.394 | 56.551 | 30.073 | 1.00 | 22.34 |
| ATOM | 889  | O    | ILE     | A | 325 | 0.238  | 55.950 | 29.209 | 1.00 | 19.22 |
| ATOM | 890  | N    | ALA     | A | 326 | -1.663 | 56.970 | 29.849 | 1.00 | 21.30 |
| ATOM | 891  | CA   | ALA     | A | 326 | -2.412 | 56.538 | 28.677 | 1.00 | 21.14 |
| ATOM | 892  | CB   | ALA     | A | 326 | -3.743 | 57.301 | 28.568 | 1.00 | 20.96 |
| ATOM | 893  | C    | ALA     | A | 326 | -1.701 | 56.616 | 27.350 | 1.00 | 20.02 |
| ATOM | 894  | O    | ALA     | A | 326 | -1.716 | 55.660 | 26.557 | 1.00 | 18.13 |
| ATOM | 895  | N    | GLU     | A | 327 | -1.087 | 57.750 | 27.055 | 1.00 | 21.17 |
| ATOM | 896  | OE2  | GLU     | A | 327 | 1.606  | 59.498 | 22.827 | 1.00 | 38.00 |
| ATOM | 897  | OE1  | GLU     | A | 327 | -0.468 | 59.073 | 22.310 | 1.00 | 37.16 |
| ATOM | 898  | CD   | GLU     | A | 327 | 0.389  | 59.482 | 23.114 | 1.00 | 35.40 |
| ATOM | 899  | CG   | GLU     | A | 327 | -0.062 | 59.993 | 24.456 | 1.00 | 33.57 |
| ATOM | 900  | CB   | GLU     | A | 327 | 0.333  | 59.223 | 25.685 | 1.00 | 26.72 |
| ATOM | 901  | CA   | GLU     | A | 327 | -0.310 | 57.845 | 25.805 | 1.00 | 23.82 |
| ATOM | 902  | C    | GLU     | A | 327 | 0.748  | 56.760 | 25.705 | 1.00 | 20.97 |
| ATOM | 903  | O    | GLU     | A | 327 | 0.932  | 56.156 | 24.626 | 1.00 | 20.68 |
| ATOM | 904  | N    | GLU     | A | 328 | 1.536  | 56.501 | 26.758 | 1.00 | 20.00 |
| ATOM | 905  | OE2  | GLU     | A | 328 | 6.485  | 57.857 | 28.558 | 1.00 | 20.00 |

|      | Atom | Type | Residue | Z | #   | X      | Y      | Z      | OCC  | B     |
|------|------|------|---------|---|-----|--------|--------|--------|------|-------|
| ATOM | 906  | OE1  | GLU     | A | 328 | 5.550  | 56.151 | 29.650 | 1.00 | 20.00 |
| ATOM | 907  | CD   | GLU     | A | 328 | 5.561  | 56.965 | 28.651 | 1.00 | 20.00 |
| ATOM | 908  | CG   | GLU     | A | 328 | 4.474  | 56.875 | 27.579 | 1.00 | 20.00 |
| ATOM | 909  | CB   | GLU     | A | 328 | 3.625  | 55.608 | 27.694 | 1.00 | 20.00 |
| ATOM | 910  | CA   | GLU     | A | 328 | 2.584  | 55.483 | 26.582 | 1.00 | 20.00 |
| ATOM | 911  | C    | GLU     | A | 328 | 1.966  | 54.088 | 26.633 | 1.00 | 20.00 |
| ATOM | 912  | O    | GLU     | A | 328 | 2.420  | 53.176 | 25.932 | 1.00 | 20.00 |
| ATOM | 913  | N    | ALA     | A | 329 | 0.930  | 53.900 | 27.438 | 1.00 | 19.57 |
| ATOM | 914  | CA   | ALA     | A | 329 | 0.280  | 52.586 | 27.501 | 1.00 | 21.09 |
| ATOM | 915  | CB   | ALA     | A | 329 | -0.828 | 52.628 | 28.545 | 1.00 | 20.52 |
| ATOM | 916  | C    | ALA     | A | 329 | -0.292 | 52.148 | 26.167 | 1.00 | 21.74 |
| ATOM | 917  | O    | ALA     | A | 329 | -0.460 | 50.963 | 25.860 | 1.00 | 22.92 |
| ATOM | 918  | N    | SER     | A | 330 | -0.593 | 53.077 | 25.263 | 1.00 | 22.47 |
| ATOM | 919  | CA   | SER     | A | 330 | -1.185 | 52.807 | 23.972 | 1.00 | 23.55 |
| ATOM | 920  | CB   | SER     | A | 330 | -1.669 | 54.151 | 23.397 | 1.00 | 23.31 |
| ATOM | 921  | OG   | SER     | A | 330 | -0.614 | 54.856 | 22.781 | 1.00 | 25.74 |
| ATOM | 922  | C    | SER     | A | 330 | -0.209 | 52.129 | 23.038 | 1.00 | 23.79 |
| ATOM | 923  | O    | SER     | A | 330 | -0.545 | 51.533 | 22.032 | 1.00 | 23.93 |
| ATOM | 924  | N    | LYS     | A | 331 | 1.073  | 52.141 | 23.385 | 1.00 | 20.00 |
| ATOM | 925  | NZ   | LYS     | A | 331 | 4.948  | 57.241 | 21.295 | 1.00 | 20.00 |
| ATOM | 926  | CE   | LYS     | A | 331 | 3.827  | 56.290 | 21.276 | 1.00 | 20.00 |
| ATOM | 927  | CD   | LYS     | A | 331 | 4.162  | 54.958 | 21.950 | 1.00 | 20.00 |
| ATOM | 928  | CG   | LYS     | A | 331 | 2.995  | 53.972 | 21.928 | 1.00 | 20.00 |
| ATOM | 929  | CB   | LYS     | A | 331 | 3.327  | 52.639 | 22.588 | 1.00 | 20.00 |
| ATOM | 930  | CA   | LYS     | A | 331 | 2.147  | 51.613 | 22.574 | 1.00 | 20.00 |
| ATOM | 931  | C    | LYS     | A | 331 | 2.659  | 50.261 | 22.982 | 1.00 | 20.00 |
| ATOM | 932  | O    | LYS     | A | 331 | 3.484  | 49.683 | 22.278 | 1.00 | 20.00 |
| ATOM | 933  | N    | VAL     | A | 332 | 2.207  | 49.748 | 24.112 | 1.00 | 21.24 |
| ATOM | 934  | CA   | VAL     | A | 332 | 2.660  | 48.458 | 24.592 | 1.00 | 19.62 |
| ATOM | 935  | CB   | VAL     | A | 332 | 3.467  | 48.639 | 25.896 | 1.00 | 20.18 |
| ATOM | 936  | CG1  | VAL     | A | 332 | 4.816  | 49.290 | 25.660 | 1.00 | 19.67 |
| ATOM | 937  | CG2  | VAL     | A | 332 | 2.651  | 49.433 | 26.897 | 1.00 | 18.82 |
| ATOM | 938  | C    | VAL     | A | 332 | 1.495  | 47.533 | 24.905 | 1.00 | 18.19 |
| ATOM | 939  | O    | VAL     | A | 332 | 0.344  | 47.965 | 24.964 | 1.00 | 18.61 |
| ATOM | 940  | N    | CYS     | A | 333 | 1.816  | 46.274 | 25.098 | 1.00 | 16.72 |
| ATOM | 941  | CA   | CYS     | A | 333 | 0.869  | 45.245 | 25.475 | 1.00 | 18.08 |
| ATOM | 942  | CB   | CYS     | A | 333 | 1.522  | 43.872 | 25.365 | 1.00 | 20.13 |
| ATOM | 943  | SG   | CYS     | A | 333 | 0.694  | 42.448 | 26.048 | 1.00 | 23.29 |
| ATOM | 944  | C    | CYS     | A | 333 | 0.346  | 45.494 | 26.878 | 1.00 | 16.83 |
| ATOM | 945  | O    | CYS     | A | 333 | -0.855 | 45.347 | 27.075 | 1.00 | 15.63 |
| ATOM | 946  | N    | LEU     | A | 334 | 1.226  | 45.820 | 27.841 | 1.00 | 12.87 |
| ATOM | 947  | CA   | LEU     | A | 334 | 0.838  | 46.094 | 29.187 | 1.00 | 12.88 |
| ATOM | 948  | CB   | LEU     | A | 334 | 0.857  | 44.925 | 30.157 | 1.00 | 13.67 |
| ATOM | 949  | CG   | LEU     | A | 334 | 0.004  | 43.686 | 29.867 | 1.00 | 12.92 |
| ATOM | 950  | CD1  | LEU     | A | 334 | 0.432  | 42.513 | 30.699 | 1.00 | 9.29  |
| ATOM | 951  | CD2  | LEU     | A | 334 | -1.465 | 44.030 | 30.158 | 1.00 | 10.80 |
| ATOM | 952  | C    | LEU     | A | 334 | 1.788  | 47.151 | 29.816 | 1.00 | 14.90 |
| ATOM | 953  | O    | LEU     | A | 334 | 2.929  | 47.313 | 29.428 | 1.00 | 13.88 |
| ATOM | 954  | N    | ALA     | A | 335 | 1.203  | 47.856 | 30.778 | 1.00 | 14.03 |
| ATOM | 955  | CA   | ALA     | A | 335 | 1.920  | 48.854 | 31.544 | 1.00 | 14.38 |
| ATOM | 956  | CB   | ALA     | A | 335 | 1.292  | 50.235 | 31.381 | 1.00 | 15.95 |
| ATOM | 957  | C    | ALA     | A | 335 | 1.859  | 48.404 | 32.991 | 1.00 | 13.27 |
| ATOM | 958  | O    | ALA     | A | 335 | 0.794  | 48.020 | 33.435 | 1.00 | 14.32 |
| ATOM | 959  | N    | HIS     | A | 336 | 2.936  | 48.458 | 33.750 | 1.00 | 12.02 |

|      | Atom | Type | Residue | Z | #   | X     | Y      | Z      | OCC  | B     |
|------|------|------|---------|---|-----|-------|--------|--------|------|-------|
| ATOM | 960  | CA   | HIS     | A | 336 | 2.886 | 49.039 | 35.141 | 1.00 | 10.67 |
| ATOM | 961  | CB   | HIS     | A | 336 | 3.543 | 46.655 | 35.252 | 1.00 | 9.55  |
| ATOM | 962  | CG   | HIS     | A | 336 | 3.104 | 45.903 | 36.449 | 1.00 | 12.03 |
| ATOM | 963  | CD2  | HIS     | A | 336 | 2.026 | 45.099 | 36.601 | 1.00 | 9.22  |
| ATOM | 964  | ND1  | HIS     | A | 336 | 3.730 | 45.915 | 37.684 | 1.00 | 11.53 |
| ATOM | 965  | CE1  | HIS     | A | 336 | 3.048 | 45.186 | 38.533 | 1.00 | 8.45  |
| ATOM | 966  | NE2  | HIS     | A | 336 | 1.995 | 44.711 | 37.891 | 1.00 | 12.17 |
| ATOM | 967  | C    | HIS     | A | 336 | 3.596 | 49.089 | 36.001 | 1.00 | 13.40 |
| ATOM | 968  | O    | HIS     | A | 336 | 4.669 | 49.576 | 35.641 | 1.00 | 13.52 |
| ATOM | 969  | N    | LEU     | A | 337 | 2.987 | 49.473 | 37.104 | 1.00 | 12.61 |
| ATOM | 970  | CA   | LEU     | A | 337 | 3.514 | 50.440 | 38.026 | 1.00 | 12.83 |
| ATOM | 971  | CB   | LEU     | A | 337 | 2.357 | 51.336 | 38.563 | 1.00 | 13.25 |
| ATOM | 972  | CG   | LEU     | A | 337 | 2.688 | 52.163 | 39.816 | 1.00 | 14.22 |
| ATOM | 973  | CD1  | LEU     | A | 337 | 3.886 | 53.054 | 39.540 | 1.00 | 14.34 |
| ATOM | 974  | CD2  | LEU     | A | 337 | 1.489 | 53.027 | 40.232 | 1.00 | 12.48 |
| ATOM | 975  | C    | LEU     | A | 337 | 4.137 | 49.730 | 39.243 | 1.00 | 11.76 |
| ATOM | 976  | O    | LEU     | A | 337 | 3.486 | 48.887 | 39.833 | 1.00 | 10.29 |
| ATOM | 977  | N    | PHE     | A | 338 | 5.396 | 50.012 | 39.548 | 1.00 | 11.12 |
| ATOM | 978  | CA   | PHE     | A | 338 | 6.001 | 49.502 | 40.775 | 1.00 | 9.77  |
| ATOM | 979  | CB   | PHE     | A | 338 | 7.378 | 48.877 | 40.584 | 1.00 | 10.95 |
| ATOM | 980  | CG   | PHE     | A | 338 | 7.336 | 47.661 | 39.688 | 1.00 | 10.01 |
| ATOM | 981  | CD1  | PHE     | A | 338 | 7.341 | 47.745 | 38.336 | 1.00 | 6.77  |
| ATOM | 982  | CD2  | PHE     | A | 338 | 7.347 | 46.392 | 40.263 | 1.00 | 10.50 |
| ATOM | 983  | CE1  | PHE     | A | 338 | 7.261 | 46.629 | 37.530 | 1.00 | 8.39  |
| ATOM | 984  | CE2  | PHE     | A | 338 | 7.260 | 45.254 | 39.504 | 1.00 | 7.33  |
| ATOM | 985  | CZ   | PHE     | A | 338 | 7.257 | 45.387 | 38.135 | 1.00 | 9.45  |
| ATOM | 986  | C    | PHE     | A | 338 | 6.093 | 50.673 | 41.742 | 1.00 | 10.02 |
| ATOM | 987  | O    | PHE     | A | 338 | 6.621 | 51.737 | 41.430 | 1.00 | 11.99 |
| ATOM | 988  | N    | THR     | A | 339 | 5.501 | 50.493 | 42.897 | 1.00 | 9.73  |
| ATOM | 989  | CA   | THR     | A | 339 | 5.455 | 51.468 | 43.940 | 1.00 | 12.72 |
| ATOM | 990  | CB   | THR     | A | 339 | 4.053 | 52.092 | 44.003 | 1.00 | 15.30 |
| ATOM | 991  | OG1  | THR     | A | 339 | 4.060 | 53.246 | 44.828 | 1.00 | 16.97 |
| ATOM | 992  | CG2  | THR     | A | 339 | 3.048 | 51.044 | 44.495 | 1.00 | 15.12 |
| ATOM | 993  | C    | THR     | A | 339 | 5.886 | 50.830 | 45.261 | 1.00 | 12.86 |
| ATOM | 994  | O    | THR     | A | 339 | 6.169 | 49.638 | 45.386 | 1.00 | 12.05 |
| ATOM | 995  | N    | TYR     | A | 340 | 5.954 | 51.663 | 46.268 | 1.00 | 11.17 |
| ATOM | 996  | CA   | TYR     | A | 340 | 6.323 | 51.315 | 47.616 | 1.00 | 11.82 |
| ATOM | 997  | CB   | TYR     | A | 340 | 7.823 | 51.632 | 47.844 | 1.00 | 10.81 |
| ATOM | 998  | CG   | TYR     | A | 340 | 8.342 | 51.050 | 49.121 | 1.00 | 11.94 |
| ATOM | 999  | CD1  | TYR     | A | 340 | 8.766 | 49.717 | 49.157 | 1.00 | 13.34 |
| ATOM | 1000 | CE1  | TYR     | A | 340 | 9.228 | 49.144 | 50.342 | 1.00 | 13.22 |
| ATOM | 1001 | CD2  | TYR     | A | 340 | 8.375 | 51.795 | 50.286 | 1.00 | 11.57 |
| ATOM | 1002 | CE2  | TYR     | A | 340 | 8.862 | 51.239 | 51.481 | 1.00 | 13.34 |
| ATOM | 1003 | CZ   | TYR     | A | 340 | 9.294 | 49.929 | 51.474 | 1.00 | 12.53 |
| ATOM | 1004 | OH   | TYR     | A | 340 | 9.708 | 49.349 | 52.630 | 1.00 | 13.01 |
| ATOM | 1005 | C    | TYR     | A | 340 | 5.422 | 52.066 | 48.560 | 1.00 | 12.56 |
| ATOM | 1006 | O    | TYR     | A | 340 | 5.784 | 53.138 | 49.086 | 1.00 | 13.24 |
| ATOM | 1007 | N    | GLN     | A | 341 | 4.248 | 51.479 | 48.801 | 1.00 | 12.63 |
| ATOM | 1008 | CA   | GLN     | A | 341 | 3.279 | 52.124 | 49.697 | 1.00 | 12.73 |
| ATOM | 1009 | CB   | GLN     | A | 341 | 2.457 | 53.199 | 48.996 | 1.00 | 15.96 |
| ATOM | 1010 | CG   | GLN     | A | 341 | 1.630 | 52.745 | 47.790 | 1.00 | 12.86 |
| ATOM | 1011 | CD   | GLN     | A | 341 | 1.063 | 53.915 | 47.015 | 1.00 | 14.37 |
| ATOM | 1012 | OE1  | GLN     | A | 341 | 0.019 | 54.455 | 47.412 | 1.00 | 14.26 |
| ATOM | 1013 | NE2  | GLN     | A | 341 | 1.690 | 54.336 | 45.913 | 1.00 | 12.87 |

|      | Atom |         |     |   |     |        |        |        |      |       |
|------|------|---------|-----|---|-----|--------|--------|--------|------|-------|
|      | Type | Residue | ?   | # | X   | Y      | Z      | OCC    | B    |       |
| ATOM | 1014 | C       | GLN | A | 341 | 2.409  | 51.026 | 50.281 | 1.00 | 13.05 |
| ATOM | 1015 | O       | GLN | A | 341 | 2.135  | 50.001 | 49.651 | 1.00 | 12.36 |
| ATOM | 1016 | N       | ASP | A | 342 | 2.036  | 51.214 | 51.518 | 1.00 | 11.62 |
| ATOM | 1017 | CA      | ASP | A | 342 | 1.313  | 50.221 | 52.293 | 1.00 | 12.36 |
| ATOM | 1018 | CB      | ASP | A | 342 | 1.766  | 50.350 | 53.748 | 1.00 | 11.58 |
| ATOM | 1019 | CG      | ASP | A | 342 | 1.603  | 49.084 | 54.533 | 1.00 | 14.83 |
| ATOM | 1020 | OD1     | ASP | A | 342 | 1.136  | 48.053 | 53.979 | 1.00 | 12.25 |
| ATOM | 1021 | OD2     | ASP | A | 342 | 1.976  | 49.034 | 55.734 | 1.00 | 16.16 |
| ATOM | 1022 | C       | ASP | A | 342 | -0.202 | 50.344 | 52.159 | 1.00 | 13.76 |
| ATOM | 1023 | O       | ASP | A | 342 | -0.850 | 50.940 | 53.016 | 1.00 | 10.06 |
| ATOM | 1024 | N       | PHE | A | 343 | -0.705 | 49.804 | 51.047 | 1.00 | 12.77 |
| ATOM | 1025 | CA      | PHE | A | 343 | -2.123 | 49.686 | 50.828 | 1.00 | 13.67 |
| ATOM | 1026 | CB      | PHE | A | 343 | -2.407 | 48.846 | 49.572 | 1.00 | 11.23 |
| ATOM | 1027 | CG      | PHE | A | 343 | -1.813 | 49.447 | 48.336 | 1.00 | 13.10 |
| ATOM | 1028 | CD1     | PHE | A | 343 | -2.070 | 50.761 | 47.978 | 1.00 | 11.42 |
| ATOM | 1029 | CD2     | PHE | A | 343 | -0.968 | 48.703 | 47.519 | 1.00 | 11.91 |
| ATOM | 1030 | CE1     | PHE | A | 343 | -1.494 | 51.298 | 46.845 | 1.00 | 11.83 |
| ATOM | 1031 | CE2     | PHE | A | 343 | -0.431 | 49.235 | 46.395 | 1.00 | 13.17 |
| ATOM | 1032 | CZ      | PHE | A | 343 | -0.693 | 50.547 | 46.011 | 1.00 | 11.97 |
| ATOM | 1033 | C       | PHE | A | 343 | -2.827 | 49.073 | 52.018 | 1.00 | 13.82 |
| ATOM | 1034 | O       | PHE | A | 343 | -2.411 | 48.111 | 52.663 | 1.00 | 11.97 |
| ATOM | 1035 | N       | ASP | A | 344 | -3.976 | 49.646 | 52.364 | 1.00 | 14.70 |
| ATOM | 1036 | CA      | ASP | A | 344 | -4.734 | 49.159 | 53.500 | 1.00 | 16.30 |
| ATOM | 1037 | CB      | ASP | A | 344 | -6.066 | 49.896 | 53.688 | 1.00 | 19.86 |
| ATOM | 1038 | CG      | ASP | A | 344 | -5.919 | 51.270 | 54.287 | 1.00 | 24.51 |
| ATOM | 1039 | OD1     | ASP | A | 344 | -4.851 | 51.804 | 54.586 | 1.00 | 24.70 |
| ATOM | 1040 | OD2     | ASP | A | 344 | -6.983 | 51.916 | 54.436 | 1.00 | 27.18 |
| ATOM | 1041 | C       | ASP | A | 344 | -5.093 | 47.675 | 53.396 | 1.00 | 13.85 |
| ATOM | 1042 | O       | ASP | A | 344 | -5.208 | 47.157 | 52.310 | 1.00 | 9.77  |
| ATOM | 1043 | N       | MET | A | 345 | -5.213 | 47.069 | 54.564 | 1.00 | 13.16 |
| ATOM | 1044 | CA      | MET | A | 345 | -5.708 | 45.753 | 54.800 | 1.00 | 17.11 |
| ATOM | 1045 | CB      | MET | A | 345 | -7.235 | 45.710 | 54.450 | 1.00 | 23.01 |
| ATOM | 1046 | CG      | MET | A | 345 | -7.944 | 46.687 | 55.406 | 1.00 | 28.99 |
| ATOM | 1047 | SD      | MET | A | 345 | -9.349 | 45.913 | 56.215 | 1.00 | 39.05 |
| ATOM | 1048 | CE      | MET | A | 345 | -9.993 | 47.308 | 57.172 | 1.00 | 36.28 |
| ATOM | 1049 | C       | MET | A | 345 | -4.992 | 44.658 | 54.023 | 1.00 | 16.11 |
| ATOM | 1050 | O       | MET | A | 345 | -5.586 | 43.729 | 53.496 | 1.00 | 11.01 |
| ATOM | 1051 | N       | GLY | A | 346 | -3.649 | 44.811 | 53.976 | 1.00 | 13.02 |
| ATOM | 1052 | CA      | GLY | A | 346 | -2.848 | 43.775 | 53.364 | 1.00 | 12.48 |
| ATOM | 1053 | C       | GLY | A | 346 | -2.754 | 43.637 | 51.897 | 1.00 | 10.57 |
| ATOM | 1054 | O       | GLY | A | 346 | -2.092 | 42.654 | 51.492 | 1.00 | 10.20 |
| ATOM | 1055 | N       | THR | A | 347 | -3.392 | 44.516 | 51.092 | 1.00 | 10.34 |
| ATOM | 1056 | CA      | THR | A | 347 | -3.236 | 44.419 | 49.645 | 1.00 | 10.83 |
| ATOM | 1057 | CB      | THR | A | 347 | -4.204 | 45.426 | 48.958 | 1.00 | 11.57 |
| ATOM | 1058 | OG1     | THR | A | 347 | -5.515 | 45.104 | 49.474 | 1.00 | 11.02 |
| ATOM | 1059 | CG2     | THR | A | 347 | -4.265 | 45.214 | 47.479 | 1.00 | 9.59  |
| ATOM | 1060 | C       | THR | A | 347 | -1.836 | 44.663 | 49.119 | 1.00 | 11.95 |
| ATOM | 1061 | O       | THR | A | 347 | -1.160 | 45.651 | 49.506 | 1.00 | 10.72 |
| ATOM | 1062 | N       | LEU | A | 348 | -1.400 | 43.853 | 48.171 | 1.00 | 9.29  |
| ATOM | 1063 | CA      | LEU | A | 348 | -0.082 | 43.950 | 47.585 | 1.00 | 11.62 |
| ATOM | 1064 | CB      | LEU | A | 348 | 0.550  | 42.518 | 47.580 | 1.00 | 11.68 |
| ATOM | 1065 | CG      | LEU | A | 348 | 0.940  | 41.992 | 48.967 | 1.00 | 13.21 |
| ATOM | 1066 | CD1     | LEU | A | 348 | 1.053  | 40.466 | 48.924 | 1.00 | 13.82 |
| ATOM | 1067 | CD2     | LEU | A | 348 | 2.282  | 42.599 | 49.398 | 1.00 | 13.80 |



|      | Atom | Type | Residue | Z | #   | X       | Y      | Z      | OCC  | B     |
|------|------|------|---------|---|-----|---------|--------|--------|------|-------|
| ATOM | 1068 | C    | LEU     | A | 348 | -0.066  | 44.478 | 46.170 | 1.00 | 10.88 |
| ATOM | 1069 | O    | LEU     | A | 348 | 0.889   | 45.107 | 45.724 | 1.00 | 10.81 |
| ATOM | 1070 | N    | GLY     | A | 349 | -1.177  | 44.229 | 45.417 | 1.00 | 10.78 |
| ATOM | 1071 | CA   | GLY     | A | 349 | -1.154  | 44.718 | 44.035 | 1.00 | 9.96  |
| ATOM | 1072 | C    | GLY     | A | 349 | -2.577  | 44.686 | 43.420 | 1.00 | 11.05 |
| ATOM | 1073 | O    | GLY     | A | 349 | -3.461  | 44.195 | 44.075 | 1.00 | 9.57  |
| ATOM | 1074 | N    | LEU     | A | 350 | -2.667  | 45.177 | 42.201 | 1.00 | 12.61 |
| ATOM | 1075 | CA   | LEU     | A | 350 | -4.033  | 45.102 | 41.592 | 1.00 | 12.78 |
| ATOM | 1076 | CB   | LEU     | A | 350 | -4.766  | 46.348 | 42.090 | 1.00 | 13.89 |
| ATOM | 1077 | CG   | LEU     | A | 350 | -6.279  | 46.356 | 41.850 | 1.00 | 16.31 |
| ATOM | 1078 | CD1  | LEU     | A | 350 | -6.981  | 45.416 | 42.807 | 1.00 | 17.00 |
| ATOM | 1079 | CD2  | LEU     | A | 350 | -6.786  | 47.797 | 41.945 | 1.00 | 15.79 |
| ATOM | 1080 | C    | LEU     | A | 350 | -3.881  | 45.086 | 40.119 | 1.00 | 10.61 |
| ATOM | 1081 | O    | LEU     | A | 350 | -2.867  | 45.625 | 39.674 | 1.00 | 9.12  |
| ATOM | 1082 | N    | ALA     | A | 351 | -4.815  | 44.544 | 39.319 | 1.00 | 8.13  |
| ATOM | 1083 | CA   | ALA     | A | 351 | -4.645  | 44.560 | 37.896 | 1.00 | 9.68  |
| ATOM | 1084 | CB   | ALA     | A | 351 | -3.807  | 43.358 | 37.429 | 1.00 | 8.30  |
| ATOM | 1085 | C    | ALA     | A | 351 | -6.006  | 44.393 | 37.158 | 1.00 | 8.00  |
| ATOM | 1086 | O    | ALA     | A | 351 | -6.781  | 43.671 | 37.749 | 1.00 | 8.17  |
| ATOM | 1087 | N    | TYR     | A | 352 | -6.102  | 44.923 | 35.997 | 1.00 | 10.56 |
| ATOM | 1088 | CA   | TYR     | A | 352 | -7.378  | 44.669 | 35.243 | 1.00 | 11.99 |
| ATOM | 1089 | CB   | TYR     | A | 352 | -7.517  | 45.727 | 34.152 | 1.00 | 13.49 |
| ATOM | 1090 | CG   | TYR     | A | 352 | -7.816  | 47.102 | 34.704 | 1.00 | 16.49 |
| ATOM | 1091 | CD1  | TYR     | A | 352 | -9.085  | 47.388 | 35.198 | 1.00 | 18.25 |
| ATOM | 1092 | CE1  | TYR     | A | 352 | -9.369  | 48.643 | 35.704 | 1.00 | 18.58 |
| ATOM | 1093 | CD2  | TYR     | A | 352 | -6.835  | 48.096 | 34.726 | 1.00 | 15.80 |
| ATOM | 1094 | CE2  | TYR     | A | 352 | -7.121  | 49.344 | 35.231 | 1.00 | 17.33 |
| ATOM | 1095 | CZ   | TYR     | A | 352 | -8.385  | 49.612 | 35.726 | 1.00 | 19.62 |
| ATOM | 1096 | OH   | TYR     | A | 352 | -8.671  | 50.865 | 36.229 | 1.00 | 20.81 |
| ATOM | 1097 | C    | TYR     | A | 352 | -7.306  | 43.297 | 34.623 | 1.00 | 11.61 |
| ATOM | 1098 | O    | TYR     | A | 352 | -6.226  | 42.856 | 34.133 | 1.00 | 9.99  |
| ATOM | 1099 | N    | VAL     | A | 353 | -8.414  | 42.569 | 34.618 | 1.00 | 9.19  |
| ATOM | 1100 | CA   | VAL     | A | 353 | -8.433  | 41.240 | 34.027 | 1.00 | 9.63  |
| ATOM | 1101 | CB   | VAL     | A | 353 | -9.532  | 40.388 | 34.675 | 1.00 | 12.16 |
| ATOM | 1102 | CG1  | VAL     | A | 353 | -9.580  | 38.963 | 34.168 | 1.00 | 11.71 |
| ATOM | 1103 | CG2  | VAL     | A | 353 | -9.337  | 40.459 | 36.180 | 1.00 | 11.77 |
| ATOM | 1104 | C    | VAL     | A | 353 | -8.597  | 41.233 | 32.532 | 1.00 | 12.50 |
| ATOM | 1105 | O    | VAL     | A | 353 | -9.522  | 41.869 | 32.012 | 1.00 | 12.29 |
| ATOM | 1106 | N    | GLY     | A | 354 | -7.759  | 40.476 | 31.830 | 1.00 | 10.94 |
| ATOM | 1107 | CA   | GLY     | A | 354 | -7.781  | 40.328 | 30.400 | 1.00 | 14.31 |
| ATOM | 1108 | C    | GLY     | A | 354 | -8.927  | 39.377 | 29.976 | 1.00 | 14.67 |
| ATOM | 1109 | O    | GLY     | A | 354 | -9.497  | 38.711 | 30.814 | 1.00 | 13.50 |
| ATOM | 1110 | N    | SER     | A | 355 | -9.183  | 39.300 | 28.685 | 1.00 | 15.31 |
| ATOM | 1111 | CA   | SER     | A | 355 | -10.226 | 38.340 | 28.254 | 1.00 | 18.47 |
| ATOM | 1112 | CB   | SER     | A | 355 | -11.596 | 39.039 | 28.449 | 1.00 | 19.00 |
| ATOM | 1113 | OG   | SER     | A | 355 | -12.631 | 38.360 | 27.760 | 1.00 | 21.32 |
| ATOM | 1114 | C    | SER     | A | 355 | -9.959  | 38.049 | 26.808 | 1.00 | 17.63 |
| ATOM | 1115 | O    | SER     | A | 355 | -9.378  | 38.937 | 26.168 | 1.00 | 18.38 |
| ATOM | 1116 | N    | PRO     | A | 356 | -10.461 | 36.952 | 26.271 | 1.00 | 19.06 |
| ATOM | 1117 | CD   | PRO     | A | 356 | -11.125 | 35.862 | 27.017 | 1.00 | 18.95 |
| ATOM | 1118 | CA   | PRO     | A | 356 | -10.370 | 36.661 | 24.859 | 1.00 | 21.26 |
| ATOM | 1119 | CB   | PRO     | A | 356 | -10.771 | 35.200 | 24.707 | 1.00 | 20.19 |
| ATOM | 1120 | CG   | PRO     | A | 356 | -11.451 | 34.834 | 25.974 | 1.00 | 20.51 |
| ATOM | 1121 | C    | PRO     | A | 356 | -11.357 | 37.502 | 24.051 | 1.00 | 24.27 |

|      | Atom<br>Type | Residue | Z | #   | X       | Y      | Z      | OCC  | B     |
|------|--------------|---------|---|-----|---------|--------|--------|------|-------|
| ATOM | 1122         | O PRO   | A | 356 | -11.249 | 37.622 | 22.833 | 1.00 | 25.16 |
| ATOM | 1123         | N ARG   | A | 357 | -12.369 | 38.028 | 24.714 | 1.00 | 27.47 |
| ATOM | 1124         | NH2 ARG | A | 357 | -14.829 | 39.823 | 29.846 | 1.00 | 45.75 |
| ATOM | 1125         | NH1 ARG | A | 357 | -15.278 | 41.187 | 28.059 | 1.00 | 45.46 |
| ATOM | 1126         | CZ ARG  | A | 357 | -15.278 | 39.980 | 28.609 | 1.00 | 43.96 |
| ATOM | 1127         | NE ARG  | A | 357 | -15.708 | 38.909 | 27.965 | 1.00 | 41.93 |
| ATOM | 1128         | CD ARG  | A | 357 | -16.239 | 38.818 | 26.627 | 1.00 | 38.04 |
| ATOM | 1129         | CG ARG  | A | 357 | -15.252 | 38.219 | 25.641 | 1.00 | 34.46 |
| ATOM | 1130         | CB ARG  | A | 357 | -14.476 | 39.345 | 24.961 | 1.00 | 32.97 |
| ATOM | 1131         | CA ARG  | A | 357 | -13.386 | 38.812 | 24.032 | 1.00 | 31.58 |
| ATOM | 1132         | C ARG   | A | 357 | -12.777 | 39.943 | 23.231 | 1.00 | 33.38 |
| ATOM | 1133         | O ARG   | A | 357 | -11.979 | 40.784 | 23.635 | 1.00 | 32.52 |
| ATOM | 1134         | CB ALA  | A | 358 | -13.971 | 40.872 | 19.874 | 1.00 | 35.32 |
| ATOM | 1135         | C ALA   | A | 358 | -12.904 | 42.350 | 21.524 | 1.00 | 36.30 |
| ATOM | 1136         | O ALA   | A | 358 | -11.940 | 43.090 | 21.425 | 1.00 | 37.79 |
| ATOM | 1137         | N ALA   | A | 358 | -13.235 | 39.948 | 21.981 | 1.00 | 35.10 |
| ATOM | 1138         | CA ALA  | A | 358 | -12.901 | 40.933 | 20.979 | 1.00 | 36.40 |
| ATOM | 1139         | N ASN   | A | 359 | -14.027 | 42.745 | 22.100 | 1.00 | 36.18 |
| ATOM | 1140         | ND2 ASN | A | 359 | -17.589 | 44.247 | 20.981 | 1.00 | 38.54 |
| ATOM | 1141         | OD1 ASN | A | 359 | -15.577 | 44.791 | 20.178 | 1.00 | 40.48 |
| ATOM | 1142         | CG ASN  | A | 359 | -16.290 | 44.493 | 21.132 | 1.00 | 39.04 |
| ATOM | 1143         | CB ASN  | A | 359 | -15.760 | 44.367 | 22.540 | 1.00 | 37.70 |
| ATOM | 1144         | CA ASN  | A | 359 | -14.263 | 44.061 | 22.641 | 1.00 | 36.27 |
| ATOM | 1145         | C ASN   | A | 359 | -13.834 | 44.198 | 24.094 | 1.00 | 35.65 |
| ATOM | 1146         | O ASN   | A | 359 | -14.157 | 45.182 | 24.751 | 1.00 | 35.92 |
| ATOM | 1147         | N SER   | A | 360 | -13.119 | 43.218 | 24.615 | 1.00 | 34.08 |
| ATOM | 1148         | OG SER  | A | 360 | -10.429 | 42.540 | 26.749 | 1.00 | 34.50 |
| ATOM | 1149         | CB SER  | A | 360 | -11.683 | 42.108 | 26.257 | 1.00 | 33.68 |
| ATOM | 1150         | CA SER  | A | 360 | -12.647 | 43.261 | 25.982 | 1.00 | 32.95 |
| ATOM | 1151         | C SER   | A | 360 | -11.907 | 44.577 | 26.260 | 1.00 | 30.62 |
| ATOM | 1152         | O SER   | A | 360 | -11.073 | 45.055 | 25.505 | 1.00 | 29.59 |
| ATOM | 1153         | N HIS   | A | 361 | -12.244 | 45.128 | 27.405 | 1.00 | 28.43 |
| ATOM | 1154         | CD2 HIS | A | 361 | -14.316 | 47.743 | 26.576 | 1.00 | 37.21 |
| ATOM | 1155         | NE2 HIS | A | 361 | -14.610 | 48.664 | 25.596 | 1.00 | 37.98 |
| ATOM | 1156         | CE1 HIS | A | 361 | -13.624 | 49.531 | 25.503 | 1.00 | 37.94 |
| ATOM | 1157         | ND1 HIS | A | 361 | -12.729 | 49.221 | 26.413 | 1.00 | 38.32 |
| ATOM | 1158         | CG HIS  | A | 361 | -13.138 | 48.108 | 27.110 | 1.00 | 36.46 |
| ATOM | 1159         | CB HIS  | A | 361 | -12.374 | 47.488 | 28.234 | 1.00 | 33.76 |
| ATOM | 1160         | CA HIS  | A | 361 | -11.550 | 46.275 | 27.920 | 1.00 | 30.24 |
| ATOM | 1161         | C HIS   | A | 361 | -10.928 | 45.653 | 29.193 | 1.00 | 29.98 |
| ATOM | 1162         | O HIS   | A | 361 | -11.660 | 45.080 | 30.014 | 1.00 | 33.02 |
| ATOM | 1163         | N GLY   | A | 362 | -9.625  | 45.543 | 29.184 | 1.00 | 25.53 |
| ATOM | 1164         | CA GLY  | A | 362 | -8.942  | 45.064 | 30.371 | 1.00 | 20.70 |
| ATOM | 1165         | C GLY   | A | 362 | -7.829  | 44.108 | 29.983 | 1.00 | 16.68 |
| ATOM | 1166         | O GLY   | A | 362 | -7.986  | 43.330 | 29.056 | 1.00 | 12.10 |
| ATOM | 1167         | N GLY   | A | 363 | -6.695  | 44.301 | 30.672 | 1.00 | 13.81 |
| ATOM | 1168         | CA GLY  | A | 363 | -5.648  | 43.339 | 30.406 | 1.00 | 14.18 |
| ATOM | 1169         | C GLY   | A | 363 | -4.908  | 43.513 | 29.110 | 1.00 | 13.66 |
| ATOM | 1170         | O GLY   | A | 363 | -4.808  | 44.608 | 28.557 | 1.00 | 12.16 |
| ATOM | 1171         | N VAL   | A | 364 | -4.310  | 42.413 | 28.673 | 1.00 | 14.17 |
| ATOM | 1172         | CG2 VAL | A | 364 | -4.030  | 40.030 | 27.062 | 1.00 | 15.53 |
| ATOM | 1173         | CG1 VAL | A | 364 | -1.902  | 40.628 | 28.266 | 1.00 | 15.36 |
| ATOM | 1174         | CB VAL  | A | 364 | -2.897  | 41.047 | 27.174 | 1.00 | 18.71 |
| ATOM | 1175         | CA VAL  | A | 364 | -3.455  | 42.442 | 27.502 | 1.00 | 17.47 |

|      | <u>Atom</u> | <u>Type</u> | <u>Residue</u> | <u>Z</u> | <u>#</u> | <u>X</u> | <u>Y</u> | <u>Z</u> | <u>OCC</u> | <u>B</u> |
|------|-------------|-------------|----------------|----------|----------|----------|----------|----------|------------|----------|
| ATOM | 1176        | C           | VAL            | A        | 364      | -4.138   | 43.070   | 26.294   | 1.00       | 22.13    |
| ATOM | 1177        | O           | VAL            | A        | 364      | -5.313   | 42.870   | 26.039   | 1.00       | 18.74    |
| ATOM | 1178        | N           | CYS            | A        | 365      | -3.323   | 43.852   | 25.611   | 1.00       | 26.09    |
| ATOM | 1179        | SG          | CYS            | A        | 365      | -3.257   | 42.201   | 22.935   | 1.00       | 38.70    |
| ATOM | 1180        | CB          | CYS            | A        | 365      | -4.184   | 43.720   | 23.283   | 1.00       | 34.15    |
| ATOM | 1181        | CA          | CYS            | A        | 365      | -3.608   | 44.572   | 24.400   | 1.00       | 32.02    |
| ATOM | 1182        | C           | CYS            | A        | 365      | -4.433   | 45.808   | 24.719   | 1.00       | 32.84    |
| ATOM | 1183        | O           | CYS            | A        | 365      | -5.505   | 45.800   | 25.307   | 1.00       | 33.41    |
| ATOM | 1184        | N           | PRO            | A        | 366      | -3.826   | 46.943   | 24.391   | 1.00       | 34.94    |
| ATOM | 1185        | CG          | PRO            | A        | 366      | -2.315   | 48.596   | 23.731   | 1.00       | 34.57    |
| ATOM | 1186        | CD          | PRO            | A        | 366      | -2.542   | 47.119   | 23.698   | 1.00       | 34.14    |
| ATOM | 1187        | CB          | PRO            | A        | 366      | -3.403   | 49.216   | 24.501   | 1.00       | 35.23    |
| ATOM | 1188        | CA          | PRO            | A        | 366      | -4.515   | 48.220   | 24.644   | 1.00       | 35.75    |
| ATOM | 1189        | C           | PRO            | A        | 366      | -5.714   | 48.244   | 23.715   | 1.00       | 36.16    |
| ATOM | 1190        | O           | PRO            | A        | 366      | -5.574   | 47.917   | 22.548   | 1.00       | 38.73    |
| ATOM | 1191        | N           | LYS            | A        | 367      | -6.905   | 48.420   | 24.211   | 1.00       | 36.55    |
| ATOM | 1192        | NZ          | LYS            | A        | 367      | -11.060  | 46.083   | 19.713   | 1.00       | 39.83    |
| ATOM | 1193        | CE          | LYS            | A        | 367      | -10.945  | 46.830   | 20.990   | 1.00       | 39.58    |
| ATOM | 1194        | CD          | LYS            | A        | 367      | -10.461  | 45.989   | 22.141   | 1.00       | 39.79    |
| ATOM | 1195        | CG          | LYS            | A        | 367      | -9.071   | 46.373   | 22.617   | 1.00       | 39.82    |
| ATOM | 1196        | CB          | LYS            | A        | 367      | -9.031   | 47.227   | 23.867   | 1.00       | 36.78    |
| ATOM | 1197        | CA          | LYS            | A        | 367      | -8.228   | 48.530   | 23.676   | 1.00       | 37.98    |
| ATOM | 1198        | C           | LYS            | A        | 367      | -8.995   | 49.679   | 24.375   | 1.00       | 36.54    |
| ATOM | 1199        | O           | LYS            | A        | 367      | -9.725   | 49.528   | 25.366   | 1.00       | 33.85    |
| ATOM | 1200        | N           | ALA            | A        | 368      | -8.855   | 50.888   | 23.839   | 1.00       | 35.07    |
| ATOM | 1201        | CA          | ALA            | A        | 368      | -9.376   | 52.113   | 24.400   | 1.00       | 32.73    |
| ATOM | 1202        | CB          | ALA            | A        | 368      | -9.170   | 53.209   | 23.330   | 1.00       | 34.00    |
| ATOM | 1203        | C           | ALA            | A        | 368      | -10.770  | 52.317   | 24.933   | 1.00       | 32.95    |
| ATOM | 1204        | O           | ALA            | A        | 368      | -11.784  | 51.928   | 24.364   | 1.00       | 32.14    |
| ATOM | 1205        | N           | TYR            | A        | 369      | -10.878  | 53.117   | 25.991   | 1.00       | 31.03    |
| ATOM | 1206        | CA          | TYR            | A        | 369      | -12.087  | 53.643   | 26.567   | 1.00       | 32.06    |
| ATOM | 1207        | CB          | TYR            | A        | 369      | -12.264  | 53.583   | 28.057   | 1.00       | 34.85    |
| ATOM | 1208        | CG          | TYR            | A        | 369      | -13.026  | 52.465   | 28.689   | 1.00       | 37.47    |
| ATOM | 1209        | CD1         | TYR            | A        | 369      | -12.349  | 51.435   | 29.321   | 1.00       | 38.45    |
| ATOM | 1210        | CE1         | TYR            | A        | 369      | -13.025  | 50.390   | 29.914   | 1.00       | 39.73    |
| ATOM | 1211        | CD2         | TYR            | A        | 369      | -14.410  | 52.415   | 28.669   | 1.00       | 39.08    |
| ATOM | 1212        | CE2         | TYR            | A        | 369      | -15.096  | 51.380   | 29.271   | 1.00       | 40.46    |
| ATOM | 1213        | CZ          | TYR            | A        | 369      | -14.397  | 50.369   | 29.891   | 1.00       | 41.04    |
| ATOM | 1214        | OH          | TYR            | A        | 369      | -15.067  | 49.320   | 30.483   | 1.00       | 42.68    |
| ATOM | 1215        | C           | TYR            | A        | 369      | -11.953  | 55.158   | 26.287   | 1.00       | 32.03    |
| ATOM | 1216        | O           | TYR            | A        | 369      | -10.842  | 55.634   | 26.529   | 1.00       | 28.95    |
| ATOM | 1217        | N           | TYR            | A        | 370      | -12.996  | 55.828   | 25.851   | 1.00       | 32.03    |
| ATOM | 1218        | OH          | TYR            | A        | 370      | -13.216  | 63.382   | 23.761   | 1.00       | 38.96    |
| ATOM | 1219        | CD2         | TYR            | A        | 370      | -14.752  | 60.205   | 24.698   | 1.00       | 36.28    |
| ATOM | 1220        | CE2         | TYR            | A        | 370      | -14.597  | 61.568   | 24.490   | 1.00       | 36.78    |
| ATOM | 1221        | CZ          | TYR            | A        | 370      | -13.409  | 62.034   | 23.975   | 1.00       | 37.70    |
| ATOM | 1222        | CE1         | TYR            | A        | 370      | -12.383  | 61.168   | 23.662   | 1.00       | 36.85    |
| ATOM | 1223        | CD1         | TYR            | A        | 370      | -12.563  | 59.820   | 23.871   | 1.00       | 35.73    |
| ATOM | 1224        | CG          | TYR            | A        | 370      | -13.741  | 59.312   | 24.388   | 1.00       | 35.35    |
| ATOM | 1225        | CB          | TYR            | A        | 370      | -13.896  | 57.816   | 24.613   | 1.00       | 34.74    |
| ATOM | 1226        | CA          | TYR            | A        | 370      | -12.850  | 57.254   | 25.574   | 1.00       | 33.23    |
| ATOM | 1227        | C           | TYR            | A        | 370      | -12.982  | 57.999   | 26.897   | 1.00       | 33.56    |
| ATOM | 1228        | O           | TYR            | A        | 370      | -13.819  | 57.580   | 27.684   | 1.00       | 33.28    |
| ATOM | 1229        | N           | SER            | A        | 371      | -12.169  | 59.015   | 27.125   | 1.00       | 35.61    |

|      | Atom | Type | Residue | Z | #   | X       | Y      | Z      | OCC  | B     |
|------|------|------|---------|---|-----|---------|--------|--------|------|-------|
| ATOM | 1230 | OG   | SER     | A | 371 | -10.952 | 60.534 | 30.263 | 1.00 | 37.79 |
| ATOM | 1231 | CB   | SER     | A | 371 | -10.994 | 59.623 | 29.183 | 1.00 | 39.02 |
| ATOM | 1232 | CA   | SER     | A | 371 | -12.297 | 59.726 | 28.389 | 1.00 | 38.04 |
| ATOM | 1233 | C    | SER     | A | 371 | -12.666 | 61.187 | 28.201 | 1.00 | 39.91 |
| ATOM | 1234 | O    | SER     | A | 371 | -11.843 | 62.022 | 27.853 | 1.00 | 38.57 |
| ATOM | 1235 | N    | PRO     | A | 372 | -13.931 | 61.484 | 28.420 | 1.00 | 43.18 |
| ATOM | 1236 | CG   | PRO     | A | 372 | -16.243 | 61.324 | 28.452 | 1.00 | 44.76 |
| ATOM | 1237 | CD   | PRO     | A | 372 | -15.008 | 60.574 | 28.867 | 1.00 | 44.03 |
| ATOM | 1238 | CB   | PRO     | A | 372 | -15.900 | 62.772 | 28.425 | 1.00 | 45.09 |
| ATOM | 1239 | CA   | PRO     | A | 372 | -14.403 | 62.878 | 28.437 | 1.00 | 45.43 |
| ATOM | 1240 | C    | PRO     | A | 372 | -13.833 | 63.366 | 29.760 | 1.00 | 46.59 |
| ATOM | 1241 | O    | PRO     | A | 372 | -14.102 | 62.743 | 30.789 | 1.00 | 47.64 |
| ATOM | 1242 | N    | VAL     | A | 373 | -12.978 | 64.362 | 29.767 | 1.00 | 48.18 |
| ATOM | 1243 | CG2  | VAL     | A | 373 | -13.693 | 65.070 | 32.937 | 1.00 | 48.74 |
| ATOM | 1244 | CG1  | VAL     | A | 373 | -11.354 | 64.454 | 33.270 | 1.00 | 48.15 |
| ATOM | 1245 | CB   | VAL     | A | 373 | -12.534 | 64.295 | 32.314 | 1.00 | 48.02 |
| ATOM | 1246 | CA   | VAL     | A | 373 | -12.176 | 64.754 | 30.916 | 1.00 | 47.53 |
| ATOM | 1247 | C    | VAL     | A | 373 | -10.843 | 64.081 | 30.527 | 1.00 | 47.84 |
| ATOM | 1248 | O    | VAL     | A | 373 | -10.706 | 62.871 | 30.685 | 1.00 | 48.07 |
| ATOM | 1249 | N    | GLY     | A | 374 | -9.966  | 64.870 | 29.936 | 1.00 | 46.71 |
| ATOM | 1250 | CA   | GLY     | A | 374 | -8.687  | 64.329 | 29.474 | 1.00 | 45.92 |
| ATOM | 1251 | C    | GLY     | A | 374 | -8.718  | 64.327 | 27.946 | 1.00 | 44.34 |
| ATOM | 1252 | O    | GLY     | A | 374 | -7.703  | 64.386 | 27.276 | 1.00 | 43.53 |
| ATOM | 1253 | N    | LYS     | A | 375 | -9.937  | 64.227 | 27.433 | 1.00 | 20.00 |
| ATOM | 1254 | NZ   | LYS     | A | 375 | -11.621 | 70.469 | 25.481 | 1.00 | 20.00 |
| ATOM | 1255 | CE   | LYS     | A | 375 | -11.822 | 69.108 | 25.996 | 1.00 | 20.00 |
| ATOM | 1256 | CD   | LYS     | A | 375 | -10.786 | 68.111 | 25.474 | 1.00 | 20.00 |
| ATOM | 1257 | CG   | LYS     | A | 375 | -10.999 | 66.697 | 26.013 | 1.00 | 20.00 |
| ATOM | 1258 | CB   | LYS     | A | 375 | -9.976  | 65.697 | 25.486 | 1.00 | 20.00 |
| ATOM | 1259 | CA   | LYS     | A | 375 | -10.201 | 64.262 | 26.011 | 1.00 | 20.00 |
| ATOM | 1260 | C    | LYS     | A | 375 | -9.308  | 63.297 | 25.260 | 1.00 | 20.00 |
| ATOM | 1261 | O    | LYS     | A | 375 | -8.529  | 63.725 | 24.411 | 1.00 | 20.00 |
| ATOM | 1262 | N    | LYS     | A | 376 | -9.386  | 62.003 | 25.604 | 1.00 | 20.00 |
| ATOM | 1263 | NZ   | LYS     | A | 376 | -3.285  | 64.692 | 24.559 | 1.00 | 20.00 |
| ATOM | 1264 | CE   | LYS     | A | 376 | -4.696  | 64.381 | 24.290 | 1.00 | 20.00 |
| ATOM | 1265 | CD   | LYS     | A | 376 | -5.139  | 63.045 | 24.890 | 1.00 | 20.00 |
| ATOM | 1266 | CG   | LYS     | A | 376 | -6.606  | 62.726 | 24.608 | 1.00 | 20.00 |
| ATOM | 1267 | CB   | LYS     | A | 376 | -7.050  | 61.390 | 25.194 | 1.00 | 20.00 |
| ATOM | 1268 | CA   | LYS     | A | 376 | -8.531  | 61.050 | 24.897 | 1.00 | 20.00 |
| ATOM | 1269 | C    | LYS     | A | 376 | -8.810  | 59.601 | 25.286 | 1.00 | 20.00 |
| ATOM | 1270 | O    | LYS     | A | 376 | -9.696  | 59.281 | 26.077 | 1.00 | 20.00 |
| ATOM | 1271 | N    | ASN     | A | 377 | -8.050  | 58.726 | 24.640 | 1.00 | 29.74 |
| ATOM | 1272 | CA   | ASN     | A | 377 | -8.240  | 57.295 | 24.862 | 1.00 | 29.33 |
| ATOM | 1273 | CB   | ASN     | A | 377 | -7.825  | 56.539 | 23.612 | 1.00 | 29.66 |
| ATOM | 1274 | CG   | ASN     | A | 377 | -8.743  | 56.803 | 22.433 | 1.00 | 30.76 |
| ATOM | 1275 | OD1  | ASN     | A | 377 | -9.964  | 56.948 | 22.559 | 1.00 | 29.66 |
| ATOM | 1276 | ND2  | ASN     | A | 377 | -8.128  | 56.865 | 21.249 | 1.00 | 31.26 |
| ATOM | 1277 | C    | ASN     | A | 377 | -7.486  | 56.848 | 26.098 | 1.00 | 28.35 |
| ATOM | 1278 | O    | ASN     | A | 377 | -6.411  | 57.376 | 26.306 | 1.00 | 26.83 |
| ATOM | 1279 | N    | ILE     | A | 378 | -8.123  | 56.055 | 26.952 | 1.00 | 26.88 |
| ATOM | 1280 | CA   | ILE     | A | 378 | -7.431  | 55.408 | 28.039 | 1.00 | 28.08 |
| ATOM | 1281 | CB   | ILE     | A | 378 | -7.802  | 55.780 | 29.473 | 1.00 | 29.37 |
| ATOM | 1282 | CG2  | ILE     | A | 378 | -7.624  | 57.282 | 29.706 | 1.00 | 28.66 |
| ATOM | 1283 | CG1  | ILE     | A | 378 | -9.217  | 55.317 | 29.789 | 1.00 | 31.06 |

|      | <u>Atom</u> | <u>Type</u> | <u>Residue</u> | <u>Z</u> | <u>#</u> | <u>X</u> | <u>Y</u> | <u>Z</u> | <u>OCC</u> | <u>B</u> |
|------|-------------|-------------|----------------|----------|----------|----------|----------|----------|------------|----------|
| ATOM | 1284        | CD1         | ILE            | A        | 378      | -9.563   | 55.301   | 31.261   | 1.00       | 32.92    |
| ATOM | 1285        | C           | ILE            | A        | 378      | -7.567   | 53.887   | 27.882   | 1.00       | 26.65    |
| ATOM | 1286        | O           | ILE            | A        | 378      | -8.559   | 53.283   | 27.479   | 1.00       | 25.21    |
| ATOM | 1287        | N           | TYR            | A        | 379      | -6.456   | 53.246   | 28.250   | 1.00       | 25.14    |
| ATOM | 1288        | CA          | TYR            | A        | 379      | -6.298   | 51.805   | 28.141   | 1.00       | 23.62    |
| ATOM | 1289        | CB          | TYR            | A        | 379      | -5.057   | 51.473   | 27.299   | 1.00       | 25.30    |
| ATOM | 1290        | CG          | TYR            | A        | 379      | -5.076   | 52.202   | 25.979   | 1.00       | 27.60    |
| ATOM | 1291        | CD1         | TYR            | A        | 379      | -4.644   | 53.523   | 25.919   | 1.00       | 28.62    |
| ATOM | 1292        | CE1         | TYR            | A        | 379      | -4.683   | 54.224   | 24.736   | 1.00       | 30.42    |
| ATOM | 1293        | CD2         | TYR            | A        | 379      | -5.571   | 51.619   | 24.836   | 1.00       | 28.58    |
| ATOM | 1294        | CE2         | TYR            | A        | 379      | -5.582   | 52.298   | 23.634   | 1.00       | 29.43    |
| ATOM | 1295        | CZ          | TYR            | A        | 379      | -5.141   | 53.597   | 23.603   | 1.00       | 30.50    |
| ATOM | 1296        | OH          | TYR            | A        | 379      | -5.162   | 54.325   | 22.441   | 1.00       | 33.44    |
| ATOM | 1297        | C           | TYR            | A        | 379      | -6.141   | 51.154   | 29.498   | 1.00       | 22.07    |
| ATOM | 1298        | O           | TYR            | A        | 379      | -5.164   | 51.460   | 30.204   | 1.00       | 22.84    |
| ATOM | 1299        | N           | LEU            | A        | 380      | -6.941   | 50.122   | 29.768   | 1.00       | 16.20    |
| ATOM | 1300        | CA          | LEU            | A        | 380      | -6.831   | 49.396   | 30.998   | 1.00       | 17.68    |
| ATOM | 1301        | CB          | LEU            | A        | 380      | -8.233   | 49.019   | 31.490   | 1.00       | 19.14    |
| ATOM | 1302        | CG          | LEU            | A        | 380      | -9.204   | 50.207   | 31.624   | 1.00       | 21.74    |
| ATOM | 1303        | CD1         | LEU            | A        | 380      | -10.479  | 49.690   | 32.285   | 1.00       | 22.06    |
| ATOM | 1304        | CD2         | LEU            | A        | 380      | -8.614   | 51.364   | 32.411   | 1.00       | 20.08    |
| ATOM | 1305        | C           | LEU            | A        | 380      | -5.903   | 48.191   | 30.845   | 1.00       | 13.92    |
| ATOM | 1306        | O           | LEU            | A        | 380      | -6.249   | 47.139   | 31.351   | 1.00       | 12.26    |
| ATOM | 1307        | N           | ASN            | A        | 381      | -4.762   | 48.385   | 30.190   | 1.00       | 14.40    |
| ATOM | 1308        | CA          | ASN            | A        | 381      | -3.798   | 47.282   | 30.009   | 1.00       | 15.71    |
| ATOM | 1309        | CB          | ASN            | A        | 381      | -3.148   | 47.364   | 28.646   | 1.00       | 13.12    |
| ATOM | 1310        | CG          | ASN            | A        | 381      | -2.442   | 48.681   | 28.373   | 1.00       | 13.93    |
| ATOM | 1311        | OD1         | ASN            | A        | 381      | -2.614   | 49.693   | 29.057   | 1.00       | 15.98    |
| ATOM | 1312        | ND2         | ASN            | A        | 381      | -1.584   | 48.766   | 27.386   | 1.00       | 13.77    |
| ATOM | 1313        | C           | ASN            | A        | 381      | -2.732   | 47.428   | 31.111   | 1.00       | 15.34    |
| ATOM | 1314        | O           | ASN            | A        | 381      | -1.538   | 47.496   | 30.826   | 1.00       | 19.25    |
| ATOM | 1315        | N           | SER            | A        | 382      | -3.178   | 47.587   | 32.318   | 1.00       | 14.28    |
| ATOM | 1316        | CA          | SER            | A        | 382      | -2.363   | 47.953   | 33.462   | 1.00       | 16.49    |
| ATOM | 1317        | CB          | SER            | A        | 382      | -2.722   | 49.449   | 33.712   | 1.00       | 19.36    |
| ATOM | 1318        | OG          | SER            | A        | 382      | -4.021   | 49.622   | 34.261   | 1.00       | 19.22    |
| ATOM | 1319        | C           | SER            | A        | 382      | -2.534   | 47.168   | 34.720   | 1.00       | 13.50    |
| ATOM | 1320        | O           | SER            | A        | 382      | -3.491   | 46.443   | 34.986   | 1.00       | 14.79    |
| ATOM | 1321        | N           | GLY            | A        | 383      | -1.543   | 47.226   | 35.602   | 1.00       | 12.08    |
| ATOM | 1322        | CA          | GLY            | A        | 383      | -1.460   | 46.552   | 36.865   | 1.00       | 7.68     |
| ATOM | 1323        | C           | GLY            | A        | 383      | -0.407   | 47.250   | 37.737   | 1.00       | 9.13     |
| ATOM | 1324        | O           | GLY            | A        | 383      | 0.356    | 48.018   | 37.167   | 1.00       | 7.23     |
| ATOM | 1325        | N           | LEU            | A        | 384      | -0.406   | 46.961   | 39.018   | 1.00       | 9.60     |
| ATOM | 1326        | CA          | LEU            | A        | 384      | 0.596    | 47.604   | 39.860   | 1.00       | 10.98    |
| ATOM | 1327        | CB          | LEU            | A        | 384      | 0.108    | 48.911   | 40.437   | 1.00       | 10.87    |
| ATOM | 1328        | CG          | LEU            | A        | 384      | -1.098   | 48.840   | 41.372   | 1.00       | 12.55    |
| ATOM | 1329        | CD1         | LEU            | A        | 384      | -0.751   | 48.583   | 42.819   | 1.00       | 11.84    |
| ATOM | 1330        | CD2         | LEU            | A        | 384      | -1.824   | 50.197   | 41.305   | 1.00       | 14.27    |
| ATOM | 1331        | C           | LEU            | A        | 384      | 0.963    | 46.614   | 40.982   | 1.00       | 11.40    |
| ATOM | 1332        | O           | LEU            | A        | 384      | 0.191    | 45.705   | 41.269   | 1.00       | 12.17    |
| ATOM | 1333        | N           | THR            | A        | 385      | 2.174    | 46.774   | 41.470   | 1.00       | 10.30    |
| ATOM | 1334        | CA          | THR            | A        | 385      | 2.773    | 45.977   | 42.535   | 1.00       | 10.05    |
| ATOM | 1335        | CB          | THR            | A        | 385      | 3.958    | 45.170   | 41.969   | 1.00       | 11.82    |
| ATOM | 1336        | OG1         | THR            | A        | 385      | 3.463    | 44.161   | 41.100   | 1.00       | 12.53    |
| ATOM | 1337        | CG2         | THR            | A        | 385      | 4.842    | 44.430   | 42.991   | 1.00       | 7.93     |

|      | Atom<br>Type | Residue | Z | #   | X      | Y      | Z      | OCC  | B     |
|------|--------------|---------|---|-----|--------|--------|--------|------|-------|
| ATOM | 1338         | C THR   | A | 385 | 3.429  | 46.936 | 43.546 | 1.00 | 10.37 |
| ATOM | 1339         | O THR   | A | 385 | 4.154  | 47.869 | 43.150 | 1.00 | 10.04 |
| ATOM | 1340         | N SER   | A | 386 | 3.153  | 46.751 | 44.806 | 1.00 | 10.16 |
| ATOM | 1341         | CA SER  | A | 386 | 3.835  | 47.470 | 45.853 | 1.00 | 12.08 |
| ATOM | 1342         | CB SER  | A | 386 | 2.913  | 47.978 | 46.925 | 1.00 | 12.65 |
| ATOM | 1343         | OG SER  | A | 386 | 3.625  | 48.590 | 47.976 | 1.00 | 12.90 |
| ATOM | 1344         | C SER   | A | 386 | 4.773  | 46.445 | 46.540 | 1.00 | 11.71 |
| ATOM | 1345         | O SER   | A | 386 | 4.348  | 45.314 | 46.714 | 1.00 | 11.70 |
| ATOM | 1346         | N THR   | A | 387 | 5.929  | 46.899 | 46.978 | 1.00 | 13.21 |
| ATOM | 1347         | CA THR  | A | 387 | 6.861  | 46.004 | 47.677 | 1.00 | 11.54 |
| ATOM | 1348         | CB THR  | A | 387 | 8.258  | 45.976 | 47.083 | 1.00 | 12.46 |
| ATOM | 1349         | OG1 THR | A | 387 | 8.794  | 47.305 | 46.902 | 1.00 | 12.52 |
| ATOM | 1350         | CG2 THR | A | 387 | 8.193  | 45.224 | 45.771 | 1.00 | 9.84  |
| ATOM | 1351         | C THR   | A | 387 | 6.917  | 46.429 | 49.137 | 1.00 | 12.59 |
| ATOM | 1352         | O THR   | A | 387 | 7.750  | 45.916 | 49.857 | 1.00 | 9.86  |
| ATOM | 1353         | N LYS   | A | 388 | 5.888  | 47.176 | 49.559 | 1.00 | 10.11 |
| ATOM | 1354         | CA LYS  | A | 388 | 5.781  | 47.451 | 50.983 | 1.00 | 11.18 |
| ATOM | 1355         | CB LYS  | A | 388 | 5.844  | 48.928 | 51.315 | 1.00 | 10.27 |
| ATOM | 1356         | CG LYS  | A | 388 | 5.598  | 49.163 | 52.809 | 1.00 | 11.78 |
| ATOM | 1357         | CD LYS  | A | 388 | 5.570  | 50.665 | 53.086 | 1.00 | 12.59 |
| ATOM | 1358         | CE LYS  | A | 388 | 5.610  | 50.846 | 54.616 | 1.00 | 12.42 |
| ATOM | 1359         | NZ LYS  | A | 388 | 5.400  | 52.289 | 54.915 | 1.00 | 12.86 |
| ATOM | 1360         | C LYS   | A | 388 | 4.466  | 46.836 | 51.470 | 1.00 | 12.79 |
| ATOM | 1361         | O LYS   | A | 388 | 3.445  | 47.068 | 50.803 | 1.00 | 13.47 |
| ATOM | 1362         | N ASN   | A | 389 | 4.490  | 46.117 | 52.561 | 1.00 | 11.20 |
| ATOM | 1363         | CA ASN  | A | 389 | 3.235  | 45.595 | 53.114 | 1.00 | 13.05 |
| ATOM | 1364         | CB ASN  | A | 389 | 2.797  | 44.247 | 52.498 | 1.00 | 9.98  |
| ATOM | 1365         | CG ASN  | A | 389 | 1.328  | 43.929 | 52.695 | 1.00 | 13.57 |
| ATOM | 1366         | OD1 ASN | A | 389 | 0.562  | 44.823 | 53.020 | 1.00 | 11.41 |
| ATOM | 1367         | ND2 ASN | A | 389 | 0.828  | 42.697 | 52.544 | 1.00 | 11.87 |
| ATOM | 1368         | C ASN   | A | 389 | 3.401  | 45.431 | 54.605 | 1.00 | 12.01 |
| ATOM | 1369         | O ASN   | A | 389 | 4.389  | 44.832 | 55.045 | 1.00 | 12.68 |
| ATOM | 1370         | N TYR   | A | 390 | 2.463  | 45.891 | 55.415 | 1.00 | 9.33  |
| ATOM | 1371         | CA TYR  | A | 390 | 2.544  | 45.725 | 56.834 | 1.00 | 11.32 |
| ATOM | 1372         | CB TYR  | A | 390 | 2.395  | 44.317 | 57.360 | 1.00 | 13.01 |
| ATOM | 1373         | CG TYR  | A | 390 | 1.034  | 43.646 | 57.138 | 1.00 | 17.63 |
| ATOM | 1374         | CD1 TYR | A | 390 | 0.888  | 42.699 | 56.135 | 1.00 | 17.99 |
| ATOM | 1375         | CE1 TYR | A | 390 | -0.324 | 42.059 | 55.906 | 1.00 | 18.34 |
| ATOM | 1376         | CD2 TYR | A | 390 | -0.059 | 43.950 | 57.918 | 1.00 | 17.56 |
| ATOM | 1377         | CE2 TYR | A | 390 | -1.295 | 43.344 | 57.684 | 1.00 | 19.81 |
| ATOM | 1378         | CZ TYR  | A | 390 | -1.408 | 42.399 | 56.685 | 1.00 | 18.72 |
| ATOM | 1379         | OH TYR  | A | 390 | -2.599 | 41.770 | 56.456 | 1.00 | 18.16 |
| ATOM | 1380         | C TYR   | A | 390 | 3.875  | 46.390 | 57.342 | 1.00 | 11.32 |
| ATOM | 1381         | O TYR   | A | 390 | 4.444  | 45.867 | 58.262 | 1.00 | 10.06 |
| ATOM | 1382         | N GLY   | A | 391 | 4.202  | 47.568 | 56.849 | 1.00 | 12.38 |
| ATOM | 1383         | CA GLY  | A | 391 | 5.264  | 48.396 | 57.395 | 1.00 | 13.46 |
| ATOM | 1384         | C GLY   | A | 391 | 6.671  | 47.822 | 57.226 | 1.00 | 14.75 |
| ATOM | 1385         | O GLY   | A | 391 | 7.615  | 48.218 | 57.920 | 1.00 | 13.47 |
| ATOM | 1386         | N LYS   | A | 392 | 6.864  | 47.001 | 56.213 | 1.00 | 14.18 |
| ATOM | 1387         | NZ LYS  | A | 392 | 6.391  | 42.087 | 59.901 | 1.00 | 31.24 |
| ATOM | 1388         | CE LYS  | A | 392 | 6.545  | 43.004 | 58.726 | 1.00 | 30.06 |
| ATOM | 1389         | CD LYS  | A | 392 | 7.980  | 43.237 | 58.298 | 1.00 | 27.75 |
| ATOM | 1390         | CG LYS  | A | 392 | 8.231  | 44.701 | 57.942 | 1.00 | 25.41 |
| ATOM | 1391         | CB LYS  | A | 392 | 8.133  | 44.929 | 56.460 | 1.00 | 20.56 |

|      | Atom |         |     |   |     |        |        |        |      |       |
|------|------|---------|-----|---|-----|--------|--------|--------|------|-------|
|      | Type | Residue | Z   | # | X   | Y      | Z      | OCC    | B    |       |
| ATOM | 1392 | CA      | LYS | A | 392 | 8.133  | 46.376 | 55.909 | 1.00 | 15.94 |
| ATOM | 1393 | C       | LYS | A | 392 | 8.265  | 46.221 | 54.399 | 1.00 | 14.65 |
| ATOM | 1394 | O       | LYS | A | 392 | 7.242  | 46.070 | 53.676 | 1.00 | 12.21 |
| ATOM | 1395 | N       | THR | A | 393 | 9.481  | 45.969 | 53.965 | 1.00 | 9.88  |
| ATOM | 1396 | CA      | THR | A | 393 | 9.744  | 45.629 | 52.574 | 1.00 | 10.28 |
| ATOM | 1397 | CB      | THR | A | 393 | 11.178 | 45.988 | 52.155 | 1.00 | 10.31 |
| ATOM | 1398 | OG1     | THR | A | 393 | 11.412 | 47.397 | 52.330 | 1.00 | 9.91  |
| ATOM | 1399 | CG2     | THR | A | 393 | 11.393 | 45.631 | 50.693 | 1.00 | 7.83  |
| ATOM | 1400 | C       | THR | A | 393 | 9.450  | 44.139 | 52.450 | 1.00 | 11.39 |
| ATOM | 1401 | O       | THR | A | 393 | 9.872  | 43.332 | 53.278 | 1.00 | 11.16 |
| ATOM | 1402 | N       | ILE | A | 394 | 8.715  | 43.737 | 51.398 | 1.00 | 8.47  |
| ATOM | 1403 | CA      | ILE | A | 394 | 8.413  | 42.305 | 51.297 | 1.00 | 8.59  |
| ATOM | 1404 | CB      | ILE | A | 394 | 7.223  | 42.076 | 50.329 | 1.00 | 7.43  |
| ATOM | 1405 | CG1     | ILE | A | 394 | 6.044  | 42.929 | 50.867 | 1.00 | 5.89  |
| ATOM | 1406 | CG2     | ILE | A | 394 | 7.562  | 42.401 | 48.910 | 1.00 | 7.72  |
| ATOM | 1407 | CD1     | ILE | A | 394 | 6.413  | 42.268 | 47.877 | 1.00 | 9.17  |
| ATOM | 1408 | C       | ILE | A | 394 | 9.657  | 41.573 | 50.761 | 1.00 | 9.33  |
| ATOM | 1409 | O       | ILE | A | 394 | 10.482 | 42.262 | 50.170 | 1.00 | 8.55  |
| ATOM | 1410 | N       | LEU | A | 395 | 9.689  | 40.276 | 50.913 | 1.00 | 7.97  |
| ATOM | 1411 | CA      | LEU | A | 395 | 10.808 | 39.499 | 50.347 | 1.00 | 11.81 |
| ATOM | 1412 | CB      | LEU | A | 395 | 10.545 | 37.998 | 50.620 | 1.00 | 12.21 |
| ATOM | 1413 | CG      | LEU | A | 395 | 10.370 | 37.651 | 52.090 | 1.00 | 13.09 |
| ATOM | 1414 | CD1     | LEU | A | 395 | 10.246 | 36.140 | 52.313 | 1.00 | 10.90 |
| ATOM | 1415 | CD2     | LEU | A | 395 | 11.569 | 38.245 | 52.832 | 1.00 | 13.70 |
| ATOM | 1416 | C       | LEU | A | 395 | 10.920 | 39.603 | 48.860 | 1.00 | 13.57 |
| ATOM | 1417 | O       | LEU | A | 395 | 9.864  | 39.692 | 48.193 | 1.00 | 11.36 |
| ATOM | 1418 | N       | THR | A | 396 | 12.089 | 39.426 | 48.281 | 1.00 | 9.31  |
| ATOM | 1419 | CA      | THR | A | 396 | 12.273 | 39.345 | 46.840 | 1.00 | 11.95 |
| ATOM | 1420 | CB      | THR | A | 396 | 13.746 | 39.021 | 46.476 | 1.00 | 14.52 |
| ATOM | 1421 | OG1     | THR | A | 396 | 14.575 | 40.034 | 47.090 | 1.00 | 16.31 |
| ATOM | 1422 | CG2     | THR | A | 396 | 13.983 | 39.148 | 44.996 | 1.00 | 16.49 |
| ATOM | 1423 | C       | THR | A | 396 | 11.376 | 38.264 | 46.209 | 1.00 | 12.19 |
| ATOM | 1424 | O       | THR | A | 396 | 10.790 | 38.544 | 45.152 | 1.00 | 11.09 |
| ATOM | 1425 | N       | LYS | A | 397 | 11.286 | 37.104 | 46.840 | 1.00 | 9.73  |
| ATOM | 1426 | CA      | LYS | A | 397 | 10.451 | 36.033 | 46.298 | 1.00 | 12.22 |
| ATOM | 1427 | CB      | LYS | A | 397 | 10.630 | 34.680 | 46.935 | 1.00 | 11.19 |
| ATOM | 1428 | CG      | LYS | A | 397 | 10.365 | 34.491 | 48.402 | 1.00 | 10.22 |
| ATOM | 1429 | CD      | LYS | A | 397 | 10.459 | 32.971 | 48.678 | 1.00 | 12.87 |
| ATOM | 1430 | CE      | LYS | A | 397 | 9.904  | 32.634 | 50.049 | 1.00 | 10.59 |
| ATOM | 1431 | NZ      | LYS | A | 397 | 10.430 | 31.409 | 50.690 | 1.00 | 13.72 |
| ATOM | 1432 | C       | LYS | A | 397 | 8.946  | 36.390 | 46.379 | 1.00 | 11.16 |
| ATOM | 1433 | O       | LYS | A | 397 | 8.250  | 35.937 | 45.488 | 1.00 | 10.09 |
| ATOM | 1434 | N       | GLU | A | 398 | 8.588  | 37.196 | 47.346 | 1.00 | 10.22 |
| ATOM | 1435 | CA      | GLU | A | 398 | 7.207  | 37.628 | 47.475 | 1.00 | 13.12 |
| ATOM | 1436 | CB      | GLU | A | 398 | 6.931  | 38.233 | 48.857 | 1.00 | 11.64 |
| ATOM | 1437 | CG      | GLU | A | 398 | 6.951  | 37.079 | 49.876 | 1.00 | 15.45 |
| ATOM | 1438 | CD      | GLU | A | 398 | 6.952  | 37.662 | 51.284 | 1.00 | 15.72 |
| ATOM | 1439 | OE1     | GLU | A | 398 | 7.139  | 38.861 | 51.557 | 1.00 | 15.77 |
| ATOM | 1440 | OE2     | GLU | A | 398 | 6.722  | 36.861 | 52.186 | 1.00 | 17.81 |
| ATOM | 1441 | C       | GLU | A | 398 | 6.875  | 38.628 | 46.374 | 1.00 | 14.23 |
| ATOM | 1442 | O       | GLU | A | 398 | 5.819  | 38.496 | 45.746 | 1.00 | 11.36 |
| ATOM | 1443 | N       | ALA | A | 399 | 7.791  | 39.566 | 46.144 | 1.00 | 11.71 |
| ATOM | 1444 | CA      | ALA | A | 399 | 7.603  | 40.571 | 45.121 | 1.00 | 10.93 |
| ATOM | 1445 | CB      | ALA | A | 399 | 8.705  | 41.611 | 45.021 | 1.00 | 10.46 |

|      | Atom |         |   |     |        |        |        |      |       |  |
|------|------|---------|---|-----|--------|--------|--------|------|-------|--|
|      | Type | Residue | Z | #   | X      | Y      | Z      | OCC  | B     |  |
| ATOM | 1446 | C ALA   | A | 399 | 7.464  | 39.901 | 43.737 | 1.00 | 11.66 |  |
| ATOM | 1447 | O ALA   | A | 399 | 6.535  | 40.310 | 43.047 | 1.00 | 8.52  |  |
| ATOM | 1448 | N ASP   | A | 400 | 8.259  | 38.892 | 43.411 | 1.00 | 10.58 |  |
| ATOM | 1449 | CA ASP  | A | 400 | 8.092  | 38.172 | 42.164 | 1.00 | 11.27 |  |
| ATOM | 1450 | CB ASP  | A | 400 | 9.061  | 37.001 | 41.994 | 1.00 | 13.33 |  |
| ATOM | 1451 | CG ASP  | A | 400 | 10.525 | 37.443 | 41.936 | 1.00 | 15.25 |  |
| ATOM | 1452 | OD1 ASP | A | 400 | 10.787 | 38.685 | 41.868 | 1.00 | 11.52 |  |
| ATOM | 1453 | OD2 ASP | A | 400 | 11.331 | 36.459 | 41.963 | 1.00 | 15.55 |  |
| ATOM | 1454 | C ASP   | A | 400 | 6.682  | 37.543 | 42.061 | 1.00 | 10.74 |  |
| ATOM | 1455 | O ASP   | A | 400 | 6.102  | 37.681 | 40.959 | 1.00 | 11.54 |  |
| ATOM | 1456 | N LEU   | A | 401 | 6.184  | 37.034 | 43.155 | 1.00 | 9.91  |  |
| ATOM | 1457 | CA LEU  | A | 401 | 4.860  | 36.399 | 43.132 | 1.00 | 12.48 |  |
| ATOM | 1458 | CB LEU  | A | 401 | 4.618  | 35.610 | 44.411 | 1.00 | 13.67 |  |
| ATOM | 1459 | CG LEU  | A | 401 | 5.551  | 34.464 | 44.805 | 1.00 | 19.11 |  |
| ATOM | 1460 | CD1 LEU | A | 401 | 5.596  | 34.451 | 46.337 | 1.00 | 20.83 |  |
| ATOM | 1461 | CD2 LEU | A | 401 | 5.072  | 33.125 | 44.302 | 1.00 | 19.44 |  |
| ATOM | 1462 | C LEU   | A | 401 | 3.724  | 37.434 | 42.994 | 1.00 | 11.96 |  |
| ATOM | 1463 | O LEU   | A | 401 | 2.701  | 37.092 | 42.388 | 1.00 | 9.62  |  |
| ATOM | 1464 | N VAL   | A | 402 | 3.849  | 38.626 | 43.576 | 1.00 | 9.23  |  |
| ATOM | 1465 | CA VAL  | A | 402 | 2.856  | 39.664 | 43.347 | 1.00 | 10.16 |  |
| ATOM | 1466 | CB VAL  | A | 402 | 3.222  | 40.976 | 44.086 | 1.00 | 11.53 |  |
| ATOM | 1467 | CG1 VAL | A | 402 | 2.219  | 42.096 | 43.805 | 1.00 | 10.53 |  |
| ATOM | 1468 | CG2 VAL | A | 402 | 3.254  | 40.598 | 45.565 | 1.00 | 8.46  |  |
| ATOM | 1469 | C VAL   | A | 402 | 2.701  | 40.016 | 41.882 | 1.00 | 12.23 |  |
| ATOM | 1470 | O VAL   | A | 402 | 1.581  | 40.096 | 41.336 | 1.00 | 9.50  |  |
| ATOM | 1471 | N THR   | A | 403 | 3.821  | 40.359 | 41.261 | 1.00 | 8.92  |  |
| ATOM | 1472 | CA THR  | A | 403 | 3.845  | 40.764 | 39.883 | 1.00 | 8.22  |  |
| ATOM | 1473 | CB THR  | A | 403 | 5.220  | 41.259 | 39.386 | 1.00 | 6.99  |  |
| ATOM | 1474 | OG1 THR | A | 403 | 5.612  | 42.325 | 40.255 | 1.00 | 6.97  |  |
| ATOM | 1475 | CG2 THR | A | 403 | 5.221  | 41.841 | 37.998 | 1.00 | 6.87  |  |
| ATOM | 1476 | C THR   | A | 403 | 3.381  | 39.610 | 38.992 | 1.00 | 9.35  |  |
| ATOM | 1477 | O THR   | A | 403 | 2.693  | 39.954 | 38.016 | 1.00 | 5.99  |  |
| ATOM | 1478 | N THR   | A | 404 | 3.855  | 38.407 | 39.301 | 1.00 | 6.34  |  |
| ATOM | 1479 | CA THR  | A | 404 | 3.382  | 37.249 | 38.521 | 1.00 | 7.96  |  |
| ATOM | 1480 | CB THR  | A | 404 | 3.962  | 35.946 | 39.104 | 1.00 | 8.71  |  |
| ATOM | 1481 | OG1 THR | A | 404 | 5.404  | 35.959 | 38.945 | 1.00 | 8.46  |  |
| ATOM | 1482 | CG2 THR | A | 404 | 3.448  | 34.743 | 38.303 | 1.00 | 8.11  |  |
| ATOM | 1483 | C THR   | A | 404 | 1.842  | 37.175 | 38.572 | 1.00 | 6.99  |  |
| ATOM | 1484 | O THR   | A | 404 | 1.211  | 36.979 | 37.529 | 1.00 | 6.33  |  |
| ATOM | 1485 | N HIS   | A | 405 | 1.298  | 37.277 | 39.751 | 1.00 | 6.76  |  |
| ATOM | 1486 | CA HIS  | A | 405 | -0.132 | 37.232 | 40.003 | 1.00 | 9.62  |  |
| ATOM | 1487 | CB HIS  | A | 405 | -0.383 | 37.343 | 41.495 | 1.00 | 7.56  |  |
| ATOM | 1488 | CG HIS  | A | 405 | -1.828 | 37.311 | 41.919 | 1.00 | 6.65  |  |
| ATOM | 1489 | CD2 HIS | A | 405 | -2.801 | 38.292 | 41.862 | 1.00 | 4.31  |  |
| ATOM | 1490 | ND1 HIS | A | 405 | -2.389 | 36.204 | 42.467 | 1.00 | 7.16  |  |
| ATOM | 1491 | CE1 HIS | A | 405 | -3.664 | 36.486 | 42.798 | 1.00 | 9.20  |  |
| ATOM | 1492 | NE2 HIS | A | 405 | -3.937 | 37.722 | 42.413 | 1.00 | 9.52  |  |
| ATOM | 1493 | C HIS   | A | 405 | -0.867 | 38.376 | 39.290 | 1.00 | 9.96  |  |
| ATOM | 1494 | O HIS   | A | 405 | -1.836 | 38.080 | 38.597 | 1.00 | 9.05  |  |
| ATOM | 1495 | N GLU   | A | 406 | -0.414 | 39.612 | 39.416 | 1.00 | 9.09  |  |
| ATOM | 1496 | CA GLU  | A | 406 | -1.106 | 40.730 | 38.755 | 1.00 | 11.72 |  |
| ATOM | 1497 | CB GLU  | A | 406 | -0.532 | 42.078 | 39.207 | 1.00 | 12.02 |  |
| ATOM | 1498 | CG GLU  | A | 406 | -0.582 | 42.239 | 40.701 | 1.00 | 11.63 |  |
| ATOM | 1499 | CD GLU  | A | 406 | -1.940 | 42.013 | 41.321 | 1.00 | 12.61 |  |



|      | Atom | Type | Residue | i | #   | X      | Y      | Z      | OCC  | B     |
|------|------|------|---------|---|-----|--------|--------|--------|------|-------|
| ATCM | 1500 | OE1  | GLU     | A | 406 | -2.985 | 42.048 | 40.632 | 1.00 | 12.02 |
| ATCM | 1501 | OE2  | GLU     | A | 406 | -1.910 | 41.759 | 42.535 | 1.00 | 12.54 |
| ATCM | 1502 | C    | GLU     | A | 406 | -1.087 | 40.659 | 37.256 | 1.00 | 13.24 |
| ATCM | 1503 | O    | GLU     | A | 406 | -2.110 | 40.827 | 36.529 | 1.00 | 10.09 |
| ATCM | 1504 | N    | LEU     | A | 407 | 0.115  | 40.341 | 36.745 | 1.00 | 9.35  |
| ATCM | 1505 | CA   | LEU     | A | 407 | 0.259  | 40.106 | 35.318 | 1.00 | 11.31 |
| ATCM | 1506 | CB   | LEU     | A | 407 | 1.702  | 39.802 | 34.937 | 1.00 | 13.34 |
| ATCM | 1507 | CG   | LEU     | A | 407 | 2.671  | 40.844 | 34.384 | 1.00 | 17.06 |
| ATCM | 1508 | CD1  | LEU     | A | 407 | 2.232  | 42.279 | 34.412 | 1.00 | 15.35 |
| ATCM | 1509 | CD2  | LEU     | A | 407 | 4.112  | 40.690 | 34.878 | 1.00 | 15.89 |
| ATCM | 1510 | C    | LEU     | A | 407 | -0.675 | 38.971 | 34.886 | 1.00 | 8.96  |
| ATCM | 1511 | O    | LEU     | A | 407 | -1.105 | 38.869 | 33.720 | 1.00 | 9.09  |
| ATCM | 1512 | N    | GLY     | A | 408 | -0.837 | 37.972 | 35.732 | 1.00 | 7.26  |
| ATCM | 1513 | CA   | GLY     | A | 408 | -1.649 | 36.774 | 35.444 | 1.00 | 7.95  |
| ATCM | 1514 | C    | GLY     | A | 408 | -3.107 | 37.247 | 35.182 | 1.00 | 8.27  |
| ATCM | 1515 | O    | GLY     | A | 408 | -3.776 | 36.757 | 34.277 | 1.00 | 7.64  |
| ATCM | 1516 | N    | HIS     | A | 409 | -3.565 | 38.171 | 36.030 | 1.00 | 10.19 |
| ATCM | 1517 | CA   | HIS     | A | 409 | -4.873 | 38.777 | 35.752 | 1.00 | 11.21 |
| ATCM | 1518 | CB   | HIS     | A | 409 | -5.162 | 39.920 | 36.713 | 1.00 | 8.68  |
| ATCM | 1519 | CG   | HIS     | A | 409 | -5.605 | 39.404 | 38.018 | 1.00 | 10.30 |
| ATCM | 1520 | CD2  | HIS     | A | 409 | -5.193 | 39.710 | 39.255 | 1.00 | 9.44  |
| ATOM | 1521 | ND1  | HIS     | A | 409 | -6.606 | 38.454 | 38.114 | 1.00 | 10.06 |
| ATOM | 1522 | CE1  | HIS     | A | 409 | -6.833 | 38.237 | 39.402 | 1.00 | 12.63 |
| ATOM | 1523 | NE2  | HIS     | A | 409 | -5.961 | 38.972 | 40.132 | 1.00 | 12.50 |
| ATOM | 1524 | C    | HIS     | A | 409 | -4.918 | 39.414 | 34.381 | 1.00 | 12.04 |
| ATOM | 1525 | O    | HIS     | A | 409 | -5.853 | 39.223 | 33.615 | 1.00 | 12.02 |
| ATOM | 1526 | N    | ASN     | A | 410 | -3.910 | 40.235 | 34.085 | 1.00 | 11.36 |
| ATOM | 1527 | CA   | ASN     | A | 410 | -3.859 | 40.925 | 32.820 | 1.00 | 10.24 |
| ATOM | 1528 | CB   | ASN     | A | 410 | -2.594 | 41.750 | 32.616 | 1.00 | 10.71 |
| ATOM | 1529 | CG   | ASN     | A | 410 | -2.499 | 43.027 | 33.424 | 1.00 | 12.40 |
| ATOM | 1530 | OD1  | ASN     | A | 410 | -1.369 | 43.394 | 33.748 | 1.00 | 9.72  |
| ATOM | 1531 | ND2  | ASN     | A | 410 | -3.598 | 43.762 | 33.714 | 1.00 | 9.17  |
| ATOM | 1532 | C    | ASN     | A | 410 | -3.953 | 39.918 | 31.675 | 1.00 | 12.78 |
| ATOM | 1533 | O    | ASN     | A | 410 | -4.538 | 40.276 | 30.652 | 1.00 | 9.40  |
| ATOM | 1534 | N    | PHE     | A | 411 | -3.292 | 38.782 | 31.796 | 1.00 | 9.09  |
| ATOM | 1535 | CA   | PHE     | A | 411 | -3.280 | 37.693 | 30.872 | 1.00 | 10.91 |
| ATOM | 1536 | CB   | PHE     | A | 411 | -2.105 | 36.703 | 31.101 | 1.00 | 10.93 |
| ATOM | 1537 | CG   | PHE     | A | 411 | -0.840 | 37.086 | 30.375 | 1.00 | 13.69 |
| ATOM | 1538 | CD1  | PHE     | A | 411 | -0.102 | 38.216 | 30.730 | 1.00 | 15.12 |
| ATOM | 1539 | CD2  | PHE     | A | 411 | -0.309 | 36.297 | 29.389 | 1.00 | 15.69 |
| ATOM | 1540 | CE1  | PHE     | A | 411 | 1.076  | 38.546 | 30.052 | 1.00 | 13.51 |
| ATOM | 1541 | CE2  | PHE     | A | 411 | 0.862  | 36.617 | 28.723 | 1.00 | 15.64 |
| ATOM | 1542 | CZ   | PHE     | A | 411 | 1.556  | 37.782 | 29.051 | 1.00 | 14.11 |
| ATOM | 1543 | C    | PHE     | A | 411 | -4.606 | 36.903 | 30.849 | 1.00 | 10.27 |
| ATOM | 1544 | O    | PHE     | A | 411 | -4.684 | 36.100 | 29.931 | 1.00 | 9.02  |
| ATOM | 1545 | N    | GLY     | A | 412 | -5.578 | 37.150 | 31.701 | 1.00 | 11.88 |
| ATOM | 1546 | CA   | GLY     | A | 412 | -6.912 | 36.517 | 31.563 | 1.00 | 11.02 |
| ATOM | 1547 | C    | GLY     | A | 412 | -7.360 | 35.734 | 32.748 | 1.00 | 12.85 |
| ATOM | 1548 | O    | GLY     | A | 412 | -8.496 | 35.256 | 32.898 | 1.00 | 11.80 |
| ATOM | 1549 | N    | ALA     | A | 413 | -6.418 | 35.577 | 33.737 | 1.00 | 9.39  |
| ATOM | 1550 | CA   | ALA     | A | 413 | -6.759 | 34.738 | 34.860 | 1.00 | 8.60  |
| ATOM | 1551 | CB   | ALA     | A | 413 | -5.523 | 34.078 | 35.504 | 1.00 | 6.06  |
| ATOM | 1552 | C    | ALA     | A | 413 | -7.520 | 35.451 | 35.966 | 1.00 | 9.94  |
| ATOM | 1553 | O    | ALA     | A | 413 | -7.216 | 36.584 | 36.300 | 1.00 | 9.19  |

|      | Atom | Type | Residue | Z | #   | X       | Y      | Z      | OCC  | B     |
|------|------|------|---------|---|-----|---------|--------|--------|------|-------|
| ATOM | 1554 | N    | GLU     | A | 414 | -8.476  | 34.694 | 36.530 | 1.00 | 9.61  |
| ATOM | 1555 | CA   | GLU     | A | 414 | -9.172  | 35.158 | 37.731 | 1.00 | 12.27 |
| ATOM | 1556 | CB   | GLU     | A | 414 | -10.666 | 34.812 | 37.677 | 1.00 | 14.74 |
| ATOM | 1557 | CG   | GLU     | A | 414 | -11.293 | 35.591 | 36.517 | 1.00 | 16.17 |
| ATOM | 1558 | CD   | GLU     | A | 414 | -11.696 | 36.987 | 36.834 | 1.00 | 20.61 |
| ATOM | 1559 | OE1  | GLU     | A | 414 | -11.520 | 37.544 | 37.933 | 1.00 | 21.11 |
| ATOM | 1560 | OE2  | GLU     | A | 414 | -12.266 | 37.646 | 35.920 | 1.00 | 24.06 |
| ATOM | 1561 | C    | GLU     | A | 414 | -8.509  | 34.457 | 38.920 | 1.00 | 12.40 |
| ATOM | 1562 | O    | GLU     | A | 414 | -7.455  | 33.841 | 38.757 | 1.00 | 12.29 |
| ATOM | 1563 | N    | HIS     | A | 415 | -9.108  | 34.478 | 40.104 | 1.00 | 11.96 |
| ATOM | 1564 | CA   | HIS     | A | 415 | -8.512  | 33.849 | 41.259 | 1.00 | 13.28 |
| ATOM | 1565 | CB   | HIS     | A | 415 | -9.093  | 34.484 | 42.514 | 1.00 | 12.84 |
| ATOM | 1566 | CG   | HIS     | A | 415 | -8.513  | 35.841 | 42.716 | 1.00 | 11.55 |
| ATOM | 1567 | CD2  | HIS     | A | 415 | -7.240  | 36.265 | 42.433 | 1.00 | 11.21 |
| ATOM | 1568 | ND1  | HIS     | A | 415 | -9.180  | 36.899 | 43.276 | 1.00 | 10.77 |
| ATOM | 1569 | CE1  | HIS     | A | 415 | -8.380  | 37.944 | 43.314 | 1.00 | 9.60  |
| ATOM | 1570 | NE2  | HIS     | A | 415 | -7.174  | 37.576 | 42.791 | 1.00 | 11.71 |
| ATOM | 1571 | C    | HIS     | A | 415 | -8.789  | 32.362 | 41.293 | 1.00 | 14.34 |
| ATOM | 1572 | O    | HIS     | A | 415 | -9.851  | 32.007 | 40.751 | 1.00 | 10.53 |
| ATOM | 1573 | N    | ASP     | A | 416 | -7.855  | 31.567 | 41.826 | 1.00 | 10.07 |
| ATOM | 1574 | CA   | ASP     | A | 416 | -8.239  | 30.158 | 41.962 | 1.00 | 11.05 |
| ATOM | 1575 | CB   | ASP     | A | 416 | -6.978  | 29.338 | 42.310 | 1.00 | 13.78 |
| ATOM | 1576 | CG   | ASP     | A | 416 | -5.913  | 29.387 | 41.229 | 1.00 | 14.67 |
| ATOM | 1577 | OD1  | ASP     | A | 416 | -6.267  | 29.373 | 40.039 | 1.00 | 13.81 |
| ATOM | 1578 | OD2  | ASP     | A | 416 | -4.717  | 29.403 | 41.608 | 1.00 | 16.01 |
| ATOM | 1579 | C    | ASP     | A | 416 | -9.254  | 29.930 | 43.052 | 1.00 | 10.40 |
| ATOM | 1580 | O    | ASP     | A | 416 | -9.169  | 30.468 | 44.159 | 1.00 | 11.17 |
| ATOM | 1581 | N    | PRO     | A | 417 | -10.296 | 29.111 | 42.805 | 1.00 | 10.30 |
| ATOM | 1582 | CD   | PRO     | A | 417 | -10.544 | 28.473 | 41.502 | 1.00 | 12.83 |
| ATOM | 1583 | CA   | PRO     | A | 417 | -11.275 | 28.774 | 43.805 | 1.00 | 12.54 |
| ATOM | 1584 | CB   | PRO     | A | 417 | -12.495 | 28.328 | 42.975 | 1.00 | 13.91 |
| ATOM | 1585 | CG   | PRO     | A | 417 | -11.940 | 27.894 | 41.674 | 1.00 | 15.31 |
| ATOM | 1586 | C    | PRO     | A | 417 | -10.837 | 27.603 | 44.689 | 1.00 | 13.42 |
| ATOM | 1587 | O    | PRO     | A | 417 | -10.002 | 26.839 | 44.276 | 1.00 | 14.77 |
| ATOM | 1588 | N    | ASP     | A | 418 | -11.346 | 27.376 | 45.860 | 1.00 | 14.02 |
| ATOM | 1589 | CA   | ASP     | A | 418 | -11.086 | 26.217 | 46.694 | 1.00 | 20.43 |
| ATOM | 1590 | CB   | ASP     | A | 418 | -11.375 | 26.531 | 48.172 | 1.00 | 22.42 |
| ATOM | 1591 | CG   | ASP     | A | 418 | -10.416 | 27.595 | 48.658 | 1.00 | 25.60 |
| ATOM | 1592 | OD1  | ASP     | A | 418 | -9.221  | 27.416 | 48.429 | 1.00 | 27.33 |
| ATOM | 1593 | OD2  | ASP     | A | 418 | -10.724 | 28.666 | 49.204 | 1.00 | 29.81 |
| ATOM | 1594 | C    | ASP     | A | 418 | -11.997 | 25.061 | 46.257 | 1.00 | 23.39 |
| ATOM | 1595 | O    | ASP     | A | 418 | -13.034 | 25.354 | 45.640 | 1.00 | 23.78 |
| ATOM | 1596 | N    | GLY     | A | 419 | -11.533 | 23.829 | 46.307 | 1.00 | 24.01 |
| ATOM | 1597 | CA   | GLY     | A | 419 | -12.290 | 22.650 | 46.050 | 1.00 | 28.51 |
| ATOM | 1598 | C    | GLY     | A | 419 | -12.000 | 21.714 | 44.916 | 1.00 | 31.09 |
| ATOM | 1599 | O    | GLY     | A | 419 | -11.000 | 21.726 | 44.169 | 1.00 | 31.19 |
| ATOM | 1600 | N    | LEU     | A | 420 | -12.976 | 20.849 | 44.625 | 1.00 | 32.09 |
| ATOM | 1601 | CD2  | LEU     | A | 420 | -14.406 | 17.142 | 44.111 | 1.00 | 38.06 |
| ATOM | 1602 | CD1  | LEU     | A | 420 | -16.571 | 18.444 | 44.050 | 1.00 | 37.27 |
| ATOM | 1603 | CG   | LEU     | A | 420 | -15.061 | 18.507 | 44.238 | 1.00 | 36.91 |
| ATOM | 1604 | CB   | LEU     | A | 420 | -14.424 | 19.470 | 43.224 | 1.00 | 36.82 |
| ATOM | 1605 | CA   | LEU     | A | 420 | -12.969 | 19.843 | 43.591 | 1.00 | 35.26 |
| ATOM | 1606 | C    | LEU     | A | 420 | -12.193 | 20.130 | 42.331 | 1.00 | 36.08 |
| ATOM | 1607 | O    | LEU     | A | 420 | -11.638 | 19.221 | 41.701 | 1.00 | 37.02 |

|      | Atom | Type | Residue | Z | #   | X       | Y      | Z      | OCC  | B     |
|------|------|------|---------|---|-----|---------|--------|--------|------|-------|
| ATOM | 1608 | N    | ALA     | A | 421 | -12.053 | 21.380 | 41.907 | 1.00 | 36.27 |
| ATOM | 1609 | CB   | ALA     | A | 421 | -11.478 | 23.254 | 40.472 | 1.00 | 37.17 |
| ATOM | 1610 | CA   | ALA     | A | 421 | -11.309 | 21.755 | 40.742 | 1.00 | 36.49 |
| ATOM | 1611 | C    | ALA     | A | 421 | -9.841  | 21.381 | 40.794 | 1.00 | 35.18 |
| ATOM | 1612 | O    | ALA     | A | 421 | -9.253  | 21.402 | 39.702 | 1.00 | 36.10 |
| ATOM | 1613 | N    | GLU     | A | 422 | -9.183  | 21.102 | 41.907 | 1.00 | 32.65 |
| ATOM | 1614 | OE2  | GLU     | A | 422 | -8.104  | 20.106 | 37.709 | 1.00 | 41.16 |
| ATOM | 1615 | OE1  | GLU     | A | 422 | -6.137  | 19.284 | 37.500 | 1.00 | 39.97 |
| ATOM | 1616 | CD   | GLU     | A | 422 | -6.983  | 19.889 | 38.198 | 1.00 | 38.24 |
| ATOM | 1617 | CG   | GLU     | A | 422 | -6.628  | 20.311 | 39.582 | 1.00 | 35.89 |
| ATOM | 1618 | CB   | GLU     | A | 422 | -7.426  | 19.813 | 40.760 | 1.00 | 31.03 |
| ATOM | 1619 | CA   | GLU     | A | 422 | -7.761  | 20.769 | 41.914 | 1.00 | 29.38 |
| ATOM | 1620 | C    | GLU     | A | 422 | -6.901  | 22.028 | 41.779 | 1.00 | 24.25 |
| ATOM | 1621 | O    | GLU     | A | 422 | -5.677  | 21.951 | 41.645 | 1.00 | 21.69 |
| ATOM | 1622 | N    | CYS     | A | 423 | -7.530  | 23.185 | 41.837 | 1.00 | 19.59 |
| ATOM | 1623 | CA   | CYS     | A | 423 | -6.862  | 24.457 | 41.613 | 1.00 | 18.31 |
| ATOM | 1624 | CB   | CYS     | A | 423 | -7.819  | 25.319 | 40.797 | 1.00 | 21.54 |
| ATOM | 1625 | SG   | CYS     | A | 423 | -8.112  | 24.725 | 39.090 | 1.00 | 22.74 |
| ATOM | 1626 | C    | CYS     | A | 423 | -6.367  | 25.102 | 42.893 | 1.00 | 16.82 |
| ATOM | 1627 | O    | CYS     | A | 423 | -5.884  | 26.233 | 42.855 | 1.00 | 14.86 |
| ATOM | 1628 | N    | ALA     | A | 424 | -6.516  | 24.451 | 44.029 | 1.00 | 15.16 |
| ATOM | 1629 | CA   | ALA     | A | 424 | -5.974  | 24.991 | 45.288 | 1.00 | 16.52 |
| ATOM | 1630 | CB   | ALA     | A | 424 | -6.940  | 25.972 | 45.924 | 1.00 | 15.07 |
| ATOM | 1631 | C    | ALA     | A | 424 | -5.603  | 23.812 | 46.165 | 1.00 | 15.42 |
| ATOM | 1632 | O    | ALA     | A | 424 | -6.206  | 23.507 | 47.182 | 1.00 | 16.31 |
| ATOM | 1633 | N    | PRO     | A | 425 | -4.545  | 23.118 | 45.774 | 1.00 | 16.63 |
| ATOM | 1634 | CD   | PRO     | A | 425 | -3.694  | 23.394 | 44.593 | 1.00 | 14.62 |
| ATOM | 1635 | CA   | PRO     | A | 425 | -4.096  | 21.935 | 46.484 | 1.00 | 18.01 |
| ATOM | 1636 | CB   | PRO     | A | 425 | -2.965  | 21.392 | 45.635 | 1.00 | 17.36 |
| ATOM | 1637 | CG   | PRO     | A | 425 | -3.064  | 22.047 | 44.301 | 1.00 | 16.07 |
| ATOM | 1638 | C    | PRO     | A | 425 | -3.655  | 22.217 | 47.908 | 1.00 | 19.52 |
| ATOM | 1639 | O    | PRO     | A | 425 | -3.304  | 23.325 | 48.294 | 1.00 | 16.80 |
| ATOM | 1640 | N    | ASN     | A | 426 | -3.670  | 21.143 | 48.707 | 1.00 | 21.90 |
| ATOM | 1641 | ND2  | ASN     | A | 426 | -6.177  | 19.346 | 50.674 | 1.00 | 32.22 |
| ATOM | 1642 | OD1  | ASN     | A | 426 | -5.934  | 21.437 | 51.378 | 1.00 | 30.53 |
| ATOM | 1643 | CG   | ASN     | A | 426 | -5.407  | 20.380 | 51.018 | 1.00 | 30.42 |
| ATOM | 1644 | CB   | ASN     | A | 426 | -3.898  | 20.167 | 50.928 | 1.00 | 27.25 |
| ATOM | 1645 | CA   | ASN     | A | 426 | -3.224  | 21.249 | 50.088 | 1.00 | 24.17 |
| ATOM | 1646 | C    | ASN     | A | 426 | -1.695  | 21.270 | 50.121 | 1.00 | 22.87 |
| ATOM | 1647 | O    | ASN     | A | 426 | -1.014  | 21.025 | 49.127 | 1.00 | 19.72 |
| ATOM | 1648 | N    | GLU     | A | 427 | -1.148  | 21.695 | 51.247 | 1.00 | 24.03 |
| ATOM | 1649 | OE2  | GLU     | A | 427 | 3.209   | 21.859 | 55.259 | 1.00 | 39.86 |
| ATOM | 1650 | OE1  | GLU     | A | 427 | 2.503   | 23.818 | 54.605 | 1.00 | 37.70 |
| ATOM | 1651 | CD   | GLU     | A | 427 | 2.640   | 22.595 | 54.427 | 1.00 | 37.41 |
| ATOM | 1652 | CG   | GLU     | A | 427 | 2.167   | 21.979 | 53.132 | 1.00 | 36.42 |
| ATOM | 1653 | CB   | GLU     | A | 427 | 0.679   | 22.110 | 52.857 | 1.00 | 32.16 |
| ATOM | 1654 | CA   | GLU     | A | 427 | 0.305   | 21.775 | 51.409 | 1.00 | 29.42 |
| ATOM | 1655 | C    | GLU     | A | 427 | 0.998   | 20.507 | 50.975 | 1.00 | 29.51 |
| ATOM | 1656 | O    | GLU     | A | 427 | 1.971   | 20.497 | 50.213 | 1.00 | 29.26 |
| ATOM | 1657 | N    | ASP     | A | 428 | 0.488   | 19.358 | 51.414 | 1.00 | 31.72 |
| ATOM | 1658 | OD2  | ASP     | A | 428 | -1.918  | 16.341 | 52.011 | 1.00 | 41.88 |
| ATOM | 1659 | OD1  | ASP     | A | 428 | -1.452  | 18.328 | 52.816 | 1.00 | 37.31 |
| ATOM | 1660 | CG   | ASP     | A | 428 | -1.103  | 17.267 | 52.267 | 1.00 | 38.88 |
| ATOM | 1661 | CB   | ASP     | A | 428 | 0.320   | 16.958 | 51.853 | 1.00 | 36.50 |

|      | Atom | Type | Residue | Z | #   | X      | Y      | Z      | OCC  | B     |
|------|------|------|---------|---|-----|--------|--------|--------|------|-------|
| ATOM | 1662 | CA   | ASP     | A | 428 | 1.042  | 18.054 | 51.077 | 1.00 | 32.85 |
| ATOM | 1663 | C    | ASP     | A | 428 | 1.081  | 17.735 | 49.610 | 1.00 | 32.15 |
| ATOM | 1664 | O    | ASP     | A | 428 | 1.827  | 16.851 | 49.173 | 1.00 | 32.63 |
| ATOM | 1665 | N    | GLN     | A | 429 | 0.302  | 18.414 | 48.772 | 1.00 | 29.90 |
| ATOM | 1666 | NE2  | GLN     | A | 429 | -0.844 | 15.151 | 46.445 | 1.00 | 35.05 |
| ATOM | 1667 | OE1  | GLN     | A | 429 | -0.895 | 15.061 | 48.694 | 1.00 | 36.32 |
| ATOM | 1668 | CD   | GLN     | A | 429 | -1.190 | 15.629 | 47.636 | 1.00 | 35.53 |
| ATOM | 1669 | CG   | GLN     | A | 429 | -1.923 | 16.955 | 47.621 | 1.00 | 32.82 |
| ATOM | 1670 | CB   | GLN     | A | 429 | -1.138 | 18.032 | 46.865 | 1.00 | 30.20 |
| ATOM | 1671 | CA   | GLN     | A | 429 | 0.307  | 18.190 | 47.347 | 1.00 | 26.44 |
| ATOM | 1672 | C    | GLN     | A | 429 | 1.041  | 19.302 | 46.621 | 1.00 | 22.82 |
| ATOM | 1673 | O    | GLN     | A | 429 | 0.832  | 19.463 | 45.426 | 1.00 | 21.67 |
| ATOM | 1674 | N    | GLY     | A | 430 | 1.812  | 20.142 | 47.320 | 1.00 | 18.52 |
| ATOM | 1675 | CA   | GLY     | A | 430 | 2.534  | 21.185 | 46.583 | 1.00 | 15.09 |
| ATOM | 1676 | C    | GLY     | A | 430 | 1.982  | 22.581 | 46.889 | 1.00 | 14.53 |
| ATOM | 1677 | O    | GLY     | A | 430 | 2.582  | 23.559 | 46.432 | 1.00 | 16.43 |
| ATOM | 1678 | N    | GLY     | A | 431 | 0.898  | 22.745 | 47.615 | 1.00 | 11.39 |
| ATOM | 1679 | CA   | GLY     | A | 431 | 0.314  | 24.011 | 47.958 | 1.00 | 12.94 |
| ATOM | 1680 | C    | GLY     | A | 431 | -0.505 | 24.702 | 46.871 | 1.00 | 10.35 |
| ATOM | 1681 | O    | GLY     | A | 431 | -0.764 | 24.181 | 45.795 | 1.00 | 11.85 |
| ATOM | 1682 | N    | LYS     | A | 432 | -0.845 | 25.936 | 47.147 | 1.00 | 11.65 |
| ATOM | 1683 | CA   | LYS     | A | 432 | -1.637 | 26.762 | 46.245 | 1.00 | 13.87 |
| ATOM | 1684 | CB   | LYS     | A | 432 | -2.343 | 27.862 | 47.049 | 1.00 | 16.54 |
| ATOM | 1685 | CG   | LYS     | A | 432 | -3.250 | 27.146 | 48.043 | 1.00 | 20.67 |
| ATOM | 1686 | CD   | LYS     | A | 432 | -4.058 | 28.036 | 48.933 | 1.00 | 24.37 |
| ATOM | 1687 | CE   | LYS     | A | 432 | -5.090 | 27.228 | 49.718 | 1.00 | 25.86 |
| ATOM | 1688 | NZ   | LYS     | A | 432 | -4.539 | 25.962 | 50.296 | 1.00 | 25.58 |
| ATOM | 1689 | C    | LYS     | A | 432 | -0.810 | 27.312 | 45.112 | 1.00 | 12.71 |
| ATOM | 1690 | O    | LYS     | A | 432 | 0.414  | 27.398 | 45.187 | 1.00 | 11.37 |
| ATOM | 1691 | N    | TYR     | A | 433 | -1.533 | 27.713 | 44.072 | 1.00 | 8.62  |
| ATOM | 1692 | CA   | TYR     | A | 433 | -0.997 | 28.243 | 42.844 | 1.00 | 8.63  |
| ATOM | 1693 | CB   | TYR     | A | 433 | -1.677 | 27.746 | 41.591 | 1.00 | 8.94  |
| ATOM | 1694 | CG   | TYR     | A | 433 | -1.507 | 26.270 | 41.276 | 1.00 | 12.81 |
| ATOM | 1695 | CD1  | TYR     | A | 433 | -2.460 | 25.350 | 41.653 | 1.00 | 12.02 |
| ATOM | 1696 | CE1  | TYR     | A | 433 | -2.310 | 23.999 | 41.361 | 1.00 | 14.63 |
| ATOM | 1697 | CD2  | TYR     | A | 433 | -0.360 | 25.813 | 40.637 | 1.00 | 13.00 |
| ATOM | 1698 | CE2  | TYR     | A | 433 | -0.202 | 24.469 | 40.333 | 1.00 | 14.04 |
| ATOM | 1699 | CZ   | TYR     | A | 433 | -1.180 | 23.579 | 40.713 | 1.00 | 15.76 |
| ATOM | 1700 | OH   | TYR     | A | 433 | -1.018 | 22.241 | 40.429 | 1.00 | 18.68 |
| ATOM | 1701 | C    | TYR     | A | 433 | -0.990 | 29.769 | 42.955 | 1.00 | 6.12  |
| ATOM | 1702 | O    | TYR     | A | 433 | -1.576 | 30.319 | 43.866 | 1.00 | 7.36  |
| ATOM | 1703 | N    | VAL     | A | 434 | -0.279 | 30.385 | 42.031 | 1.00 | 8.06  |
| ATOM | 1704 | CA   | VAL     | A | 434 | -0.023 | 31.820 | 42.080 | 1.00 | 9.13  |
| ATOM | 1705 | CB   | VAL     | A | 434 | 1.026  | 32.189 | 41.035 | 1.00 | 9.24  |
| ATOM | 1706 | CG1  | VAL     | A | 434 | 0.473  | 32.255 | 39.614 | 1.00 | 9.78  |
| ATOM | 1707 | CG2  | VAL     | A | 434 | 1.656  | 33.531 | 41.432 | 1.00 | 9.67  |
| ATOM | 1708 | C    | VAL     | A | 434 | -1.247 | 32.724 | 41.971 | 1.00 | 9.44  |
| ATOM | 1709 | O    | VAL     | A | 434 | -1.224 | 33.807 | 42.521 | 1.00 | 8.77  |
| ATOM | 1710 | N    | MET     | A | 435 | -2.348 | 32.242 | 41.373 | 1.00 | 9.61  |
| ATOM | 1711 | CA   | MET     | A | 435 | -3.580 | 33.044 | 41.377 | 1.00 | 10.35 |
| ATOM | 1712 | CB   | MET     | A | 435 | -4.313 | 32.866 | 40.054 | 1.00 | 9.92  |
| ATOM | 1713 | CG   | MET     | A | 435 | -3.514 | 33.300 | 38.848 | 1.00 | 10.91 |
| ATOM | 1714 | SD   | MET     | A | 435 | -2.789 | 34.945 | 38.866 | 1.00 | 11.06 |
| ATOM | 1715 | CE   | MET     | A | 435 | -4.229 | 35.954 | 39.266 | 1.00 | 11.66 |

|      | <u>Atom</u> | <u>Type</u> | <u>Residue</u> | <u>Z</u> | <u>#</u> | <u>X</u> | <u>Y</u> | <u>Z</u> | <u>OCC</u> | <u>B</u> |
|------|-------------|-------------|----------------|----------|----------|----------|----------|----------|------------|----------|
| ATOM | 1716        | C           | MET            | A        | 435      | -4.479   | 32.835   | 42.569   | 1.00       | 11.89    |
| ATOM | 1717        | O           | MET            | A        | 435      | -5.625   | 33.382   | 42.578   | 1.00       | 10.19    |
| ATOM | 1718        | N           | TYR            | A        | 436      | -4.004   | 32.200   | 43.636   | 1.00       | 9.70     |
| ATOM | 1719        | CA          | TYR            | A        | 436      | -4.776   | 32.133   | 44.873   | 1.00       | 10.59    |
| ATOM | 1720        | CB          | TYR            | A        | 436      | -4.154   | 31.274   | 45.976   | 1.00       | 12.19    |
| ATOM | 1721        | CG          | TYR            | A        | 436      | -5.187   | 30.700   | 46.929   | 1.00       | 12.41    |
| ATOM | 1722        | CD1         | TYR            | A        | 436      | -6.086   | 29.710   | 46.528   | 1.00       | 13.54    |
| ATOM | 1723        | CE1         | TYR            | A        | 436      | -7.026   | 29.190   | 47.405   | 1.00       | 10.84    |
| ATOM | 1724        | CD2         | TYR            | A        | 436      | -5.275   | 31.200   | 48.218   | 1.00       | 12.72    |
| ATOM | 1725        | CE2         | TYR            | A        | 436      | -6.216   | 30.710   | 49.104   | 1.00       | 15.95    |
| ATOM | 1726        | CZ          | TYR            | A        | 436      | -7.105   | 29.725   | 48.659   | 1.00       | 14.43    |
| ATOM | 1727        | OH          | TYR            | A        | 436      | -8.012   | 29.268   | 49.572   | 1.00       | 17.14    |
| ATOM | 1728        | C           | TYR            | A        | 436      | -4.977   | 33.571   | 45.304   | 1.00       | 10.80    |
| ATOM | 1729        | O           | TYR            | A        | 436      | -4.106   | 34.412   | 45.121   | 1.00       | 7.79     |
| ATOM | 1730        | N           | PRO            | A        | 437      | -6.178   | 33.938   | 45.778   | 1.00       | 11.93    |
| ATOM | 1731        | CD          | PRO            | A        | 437      | -7.340   | 33.037   | 45.939   | 1.00       | 11.26    |
| ATOM | 1732        | CA          | PRO            | A        | 437      | -6.467   | 35.326   | 46.139   | 1.00       | 10.62    |
| ATOM | 1733        | CB          | PRO            | A        | 437      | -7.962   | 35.319   | 46.495   | 1.00       | 12.25    |
| ATOM | 1734        | CG          | PRO            | A        | 437      | -8.320   | 33.884   | 46.714   | 1.00       | 12.44    |
| ATOM | 1735        | C           | PRO            | A        | 437      | -5.713   | 35.775   | 47.385   | 1.00       | 10.79    |
| ATOM | 1736        | O           | PRO            | A        | 437      | -5.577   | 36.995   | 47.602   | 1.00       | 11.50    |
| ATOM | 1737        | N           | ILE            | A        | 438      | -5.411   | 34.802   | 48.243   | 1.00       | 11.06    |
| ATOM | 1738        | CA          | ILE            | A        | 438      | -4.645   | 35.046   | 49.464   | 1.00       | 14.21    |
| ATOM | 1739        | CB          | ILE            | A        | 438      | -5.154   | 34.201   | 50.625   | 1.00       | 16.10    |
| ATOM | 1740        | CG2         | ILE            | A        | 438      | -4.290   | 34.449   | 51.876   | 1.00       | 19.74    |
| ATOM | 1741        | CG1         | ILE            | A        | 438      | -6.619   | 34.470   | 50.967   | 1.00       | 19.29    |
| ATOM | 1742        | CD1         | ILE            | A        | 438      | -7.175   | 33.545   | 52.055   | 1.00       | 20.13    |
| ATOM | 1743        | C           | ILE            | A        | 438      | -3.173   | 34.778   | 49.119   | 1.00       | 14.66    |
| ATOM | 1744        | O           | ILE            | A        | 438      | -2.796   | 33.666   | 48.710   | 1.00       | 10.76    |
| ATOM | 1745        | N           | ALA            | A        | 439      | -2.342   | 35.803   | 49.202   | 1.00       | 12.90    |
| ATOM | 1746        | CB          | ALA            | A        | 439      | -0.137   | 36.968   | 49.129   | 1.00       | 13.51    |
| ATOM | 1747        | CA          | ALA            | A        | 439      | -0.946   | 35.702   | 48.748   | 1.00       | 12.56    |
| ATOM | 1748        | C           | ALA            | A        | 439      | -0.219   | 34.450   | 49.179   | 1.00       | 11.82    |
| ATOM | 1749        | O           | ALA            | A        | 439      | -0.053   | 34.221   | 50.350   | 1.00       | 12.72    |
| ATOM | 1750        | N           | VAL            | A        | 440      | 0.244    | 33.624   | 48.232   | 1.00       | 12.54    |
| ATOM | 1751        | CA          | VAL            | A        | 440      | 1.038    | 32.460   | 48.610   | 1.00       | 13.18    |
| ATOM | 1752        | CB          | VAL            | A        | 440      | 1.194    | 31.545   | 47.405   | 1.00       | 13.89    |
| ATOM | 1753        | CG1         | VAL            | A        | 440      | -0.203   | 30.964   | 47.060   | 1.00       | 14.71    |
| ATOM | 1754        | CG2         | VAL            | A        | 440      | 1.748    | 32.335   | 46.225   | 1.00       | 14.29    |
| ATOM | 1755        | C           | VAL            | A        | 440      | 2.422    | 32.915   | 49.105   | 1.00       | 13.24    |
| ATOM | 1756        | O           | VAL            | A        | 440      | 2.951    | 33.937   | 48.665   | 1.00       | 10.97    |
| ATOM | 1757        | N           | SER            | A        | 441      | 3.009    | 32.117   | 49.958   | 1.00       | 13.77    |
| ATOM | 1758        | CA          | SER            | A        | 441      | 4.320    | 32.448   | 50.541   | 1.00       | 15.67    |
| ATOM | 1759        | CB          | SER            | A        | 441      | 4.602    | 31.531   | 51.741   | 1.00       | 14.54    |
| ATOM | 1760        | OG          | SER            | A        | 441      | 4.895    | 30.230   | 51.251   | 1.00       | 12.13    |
| ATOM | 1761        | C           | SER            | A        | 441      | 5.443    | 32.298   | 49.543   | 1.00       | 14.86    |
| ATOM | 1762        | O           | SER            | A        | 441      | 6.393    | 33.042   | 49.627   | 1.00       | 16.15    |
| ATOM | 1763        | N           | GLY            | A        | 442      | 5.365    | 31.340   | 48.626   | 1.00       | 15.69    |
| ATOM | 1764        | CA          | GLY            | A        | 442      | 6.458    | 31.086   | 47.680   | 1.00       | 15.78    |
| ATOM | 1765        | C           | GLY            | A        | 442      | 7.329    | 29.955   | 48.292   | 1.00       | 17.87    |
| ATOM | 1766        | O           | GLY            | A        | 442      | 8.313    | 29.533   | 47.700   | 1.00       | 17.88    |
| ATOM | 1767        | N           | ASP            | A        | 443      | 6.933    | 29.420   | 49.433   | 1.00       | 16.97    |
| ATOM | 1768        | CA          | ASP            | A        | 443      | 7.639    | 28.297   | 50.053   | 1.00       | 19.48    |
| ATOM | 1769        | CB          | ASP            | A        | 443      | 7.315    | 28.159   | 51.522   | 1.00       | 20.17    |

|      | <u>Atom</u> | <u>Type</u> | <u>Residue</u> | <u>Z</u> | <u>#</u> | <u>X</u> | <u>Y</u> | <u>Z</u> | <u>OCC</u> | <u>B</u> |
|------|-------------|-------------|----------------|----------|----------|----------|----------|----------|------------|----------|
| ATOM | 1770        | CG          | ASP            | A        | 443      | 7.612    | 29.371   | 52.357   | 1.00       | 23.62    |
| ATOM | 1771        | OD1         | ASP            | A        | 443      | 8.296    | 30.306   | 51.896   | 1.00       | 23.81    |
| ATOM | 1772        | OD2         | ASP            | A        | 443      | 7.119    | 29.399   | 53.505   | 1.00       | 25.54    |
| ATOM | 1773        | C           | ASP            | A        | 443      | 7.308    | 26.945   | 49.435   | 1.00       | 21.78    |
| ATOM | 1774        | O           | ASP            | A        | 443      | 8.052    | 25.962   | 49.619   | 1.00       | 20.22    |
| ATOM | 1775        | N           | HIS            | A        | 444      | 6.163    | 26.878   | 48.737   | 1.00       | 18.42    |
| ATOM | 1776        | CA          | HIS            | A        | 444      | 5.734    | 25.593   | 48.195   | 1.00       | 18.25    |
| ATOM | 1777        | CB          | HIS            | A        | 444      | 4.263    | 25.329   | 48.628   | 1.00       | 19.33    |
| ATOM | 1778        | CG          | HIS            | A        | 444      | 4.010    | 25.631   | 50.066   | 1.00       | 21.40    |
| ATOM | 1779        | CD2         | HIS            | A        | 444      | 3.475    | 26.703   | 50.697   | 1.00       | 21.56    |
| ATOM | 1780        | ND1         | HIS            | A        | 444      | 4.407    | 24.766   | 51.066   | 1.00       | 22.82    |
| ATOM | 1781        | CE1         | HIS            | A        | 444      | 4.098    | 25.274   | 52.242   | 1.00       | 22.65    |
| ATOM | 1782        | NE2         | HIS            | A        | 444      | 3.540    | 26.457   | 52.047   | 1.00       | 23.53    |
| ATOM | 1783        | C           | HIS            | A        | 444      | 5.869    | 25.478   | 46.699   | 1.00       | 18.20    |
| ATOM | 1784        | O           | HIS            | A        | 444      | 5.869    | 26.430   | 45.924   | 1.00       | 16.89    |
| ATOM | 1785        | N           | GLU            | A        | 445      | 5.967    | 24.246   | 46.228   | 1.00       | 18.90    |
| ATOM | 1786        | OE2         | GLU            | A        | 445      | 7.287    | 19.466   | 44.909   | 1.00       | 37.32    |
| ATOM | 1787        | OE1         | GLU            | A        | 445      | 5.382    | 19.436   | 43.805   | 1.00       | 36.75    |
| ATOM | 1788        | CD          | GLU            | A        | 445      | 6.406    | 20.025   | 44.213   | 1.00       | 34.73    |
| ATOM | 1789        | CG          | GLU            | A        | 445      | 6.551    | 21.509   | 43.912   | 1.00       | 31.48    |
| ATOM | 1790        | CB          | GLU            | A        | 445      | 5.641    | 22.370   | 44.753   | 1.00       | 24.36    |
| ATOM | 1791        | CA          | GLU            | A        | 445      | 6.094    | 23.856   | 44.844   | 1.00       | 21.30    |
| ATOM | 1792        | C           | GLU            | A        | 445      | 5.192    | 24.573   | 43.856   | 1.00       | 19.12    |
| ATOM | 1793        | O           | GLU            | A        | 445      | 5.654    | 25.106   | 42.852   | 1.00       | 18.43    |
| ATOM | 1794        | N           | ASN            | A        | 446      | 3.886    | 24.568   | 44.155   | 1.00       | 14.02    |
| ATOM | 1795        | CA          | ASN            | A        | 446      | 2.931    | 25.161   | 43.217   | 1.00       | 12.89    |
| ATOM | 1796        | CB          | ASN            | A        | 446      | 1.558    | 24.575   | 43.616   | 1.00       | 13.52    |
| ATOM | 1797        | CG          | ASN            | A        | 446      | 1.492    | 23.081   | 43.416   | 1.00       | 11.57    |
| ATOM | 1798        | OD1         | ASN            | A        | 446      | 2.288    | 22.530   | 42.688   | 1.00       | 14.69    |
| ATOM | 1799        | ND2         | ASN            | A        | 446      | 0.580    | 22.359   | 44.016   | 1.00       | 14.47    |
| ATOM | 1800        | C           | ASN            | A        | 446      | 2.880    | 26.669   | 43.236   | 1.00       | 12.30    |
| ATOM | 1801        | O           | ASN            | A        | 446      | 2.299    | 27.295   | 42.349   | 1.00       | 11.18    |
| ATOM | 1802        | N           | ASN            | A        | 447      | 3.432    | 27.299   | 44.274   | 1.00       | 12.22    |
| ATOM | 1803        | CA          | ASN            | A        | 447      | 3.261    | 28.692   | 44.560   | 1.00       | 12.81    |
| ATOM | 1804        | CB          | ASN            | A        | 447      | 3.943    | 29.244   | 45.794   | 1.00       | 13.02    |
| ATOM | 1805        | CG          | ASN            | A        | 447      | 3.432    | 28.721   | 47.094   | 1.00       | 14.61    |
| ATOM | 1806        | OD1         | ASN            | A        | 447      | 4.151    | 28.922   | 48.081   | 1.00       | 15.02    |
| ATOM | 1807        | ND2         | ASN            | A        | 447      | 2.276    | 28.070   | 47.103   | 1.00       | 13.05    |
| ATOM | 1808        | C           | ASN            | A        | 447      | 3.662    | 29.596   | 43.403   | 1.00       | 14.50    |
| ATOM | 1809        | O           | ASN            | A        | 447      | 2.990    | 30.597   | 43.173   | 1.00       | 14.90    |
| ATOM | 1810        | N           | LYS            | A        | 448      | 4.698    | 29.182   | 42.678   | 1.00       | 15.41    |
| ATOM | 1811        | CA          | LYS            | A        | 448      | 5.123    | 30.032   | 41.582   | 1.00       | 19.44    |
| ATOM | 1812        | CB          | LYS            | A        | 448      | 6.678    | 30.007   | 41.496   | 1.00       | 20.29    |
| ATOM | 1813        | CG          | LYS            | A        | 448      | 7.319    | 30.599   | 42.725   | 1.00       | 22.70    |
| ATOM | 1814        | CD          | LYS            | A        | 448      | 8.503    | 31.527   | 42.408   | 1.00       | 25.96    |
| ATOM | 1815        | CE          | LYS            | A        | 448      | 8.285    | 32.968   | 42.835   | 1.00       | 24.34    |
| ATOM | 1816        | NZ          | LYS            | A        | 448      | 8.963    | 33.438   | 44.090   | 1.00       | 16.70    |
| ATOM | 1817        | C           | LYS            | A        | 448      | 4.568    | 29.566   | 40.271   | 1.00       | 19.62    |
| ATOM | 1818        | O           | LYS            | A        | 448      | 5.136    | 29.990   | 39.263   | 1.00       | 25.92    |
| ATOM | 1819        | N           | MET            | A        | 449      | 3.632    | 28.647   | 40.230   | 1.00       | 13.54    |
| ATOM | 1820        | CA          | MET            | A        | 449      | 3.122    | 28.149   | 38.956   | 1.00       | 14.78    |
| ATOM | 1821        | CB          | MET            | A        | 449      | 3.181    | 26.610   | 39.000   | 1.00       | 17.23    |
| ATOM | 1822        | CG          | MET            | A        | 449      | 4.638    | 26.182   | 39.231   | 1.00       | 23.71    |
| ATOM | 1823        | SD          | MET            | A        | 449      | 5.557    | 26.266   | 37.701   | 1.00       | 35.18    |

|      | Atom | Type | Residue | Z | #   | X       | Y      | Z      | OCC  | B     |
|------|------|------|---------|---|-----|---------|--------|--------|------|-------|
| ATOM | 1824 | CE   | MET     | A | 449 | 6.512   | 27.753 | 37.876 | 1.00 | 29.45 |
| ATOM | 1825 | C    | MET     | A | 449 | 1.660   | 28.558 | 38.779 | 1.00 | 10.74 |
| ATOM | 1826 | O    | MET     | A | 449 | 1.051   | 28.898 | 39.776 | 1.00 | 7.03  |
| ATOM | 1827 | N    | PHE     | A | 450 | 1.104   | 28.330 | 37.629 | 1.00 | 9.72  |
| ATOM | 1828 | CA   | PHE     | A | 450 | -0.319  | 28.583 | 37.393 | 1.00 | 11.38 |
| ATOM | 1829 | CB   | PHE     | A | 450 | -0.503  | 29.170 | 35.975 | 1.00 | 11.13 |
| ATOM | 1830 | CG   | PHE     | A | 450 | -0.071  | 30.631 | 35.959 | 1.00 | 12.52 |
| ATOM | 1831 | CD1  | PHE     | A | 450 | -0.930  | 31.655 | 36.320 | 1.00 | 12.19 |
| ATOM | 1832 | CD2  | PHE     | A | 450 | 1.207   | 30.955 | 35.549 | 1.00 | 10.84 |
| ATOM | 1833 | CE1  | PHE     | A | 450 | -0.508  | 32.973 | 36.265 | 1.00 | 11.08 |
| ATOM | 1834 | CE2  | PHE     | A | 450 | 1.624   | 32.264 | 35.490 | 1.00 | 10.58 |
| ATOM | 1835 | CZ   | PHE     | A | 450 | 0.770   | 33.283 | 35.856 | 1.00 | 10.00 |
| ATOM | 1836 | C    | PHE     | A | 450 | -1.150  | 27.312 | 37.490 | 1.00 | 11.07 |
| ATOM | 1837 | O    | PHE     | A | 450 | -0.799  | 26.260 | 36.954 | 1.00 | 9.07  |
| ATOM | 1838 | N    | SER     | A | 451 | -2.323  | 27.410 | 38.138 | 1.00 | 11.36 |
| ATOM | 1839 | CA   | SER     | A | 451 | -3.268  | 26.315 | 38.270 | 1.00 | 10.14 |
| ATOM | 1840 | CB   | SER     | A | 451 | -4.487  | 26.735 | 39.155 | 1.00 | 10.95 |
| ATOM | 1841 | OG   | SER     | A | 451 | -5.179  | 27.782 | 38.420 | 1.00 | 9.02  |
| ATOM | 1842 | C    | SER     | A | 451 | -3.844  | 25.958 | 36.901 | 1.00 | 9.35  |
| ATOM | 1843 | O    | SER     | A | 451 | -3.770  | 26.735 | 35.963 | 1.00 | 9.40  |
| ATOM | 1844 | N    | GLN     | A | 452 | -4.577  | 24.855 | 36.824 | 1.00 | 12.16 |
| ATOM | 1845 | CA   | GLN     | A | 452 | -5.351  | 24.521 | 35.618 | 1.00 | 13.47 |
| ATOM | 1846 | CB   | GLN     | A | 452 | -5.964  | 23.125 | 35.803 | 1.00 | 16.94 |
| ATOM | 1847 | CG   | GLN     | A | 452 | -6.700  | 22.595 | 34.601 | 1.00 | 21.50 |
| ATOM | 1848 | CD   | GLN     | A | 452 | -5.827  | 22.669 | 33.361 | 1.00 | 23.04 |
| ATOM | 1849 | OE1  | GLN     | A | 452 | -4.673  | 22.244 | 33.400 | 1.00 | 21.47 |
| ATOM | 1850 | NE2  | GLN     | A | 452 | -6.377  | 23.285 | 32.307 | 1.00 | 23.25 |
| ATOM | 1851 | C    | GLN     | A | 452 | -6.430  | 25.554 | 35.338 | 1.00 | 13.65 |
| ATOM | 1852 | O    | GLN     | A | 452 | -6.638  | 25.907 | 34.165 | 1.00 | 14.17 |
| ATOM | 1853 | N    | CYS     | A | 453 | -7.045  | 26.104 | 36.363 | 1.00 | 14.02 |
| ATOM | 1854 | CA   | CYS     | A | 453 | -8.092  | 27.127 | 36.197 | 1.00 | 17.31 |
| ATOM | 1855 | CB   | CYS     | A | 453 | -8.719  | 27.417 | 37.560 | 1.00 | 21.49 |
| ATOM | 1856 | SG   | CYS     | A | 453 | -9.533  | 26.093 | 38.447 | 1.00 | 29.58 |
| ATOM | 1857 | C    | CYS     | A | 453 | -7.500  | 28.361 | 35.535 | 1.00 | 15.91 |
| ATOM | 1858 | O    | CYS     | A | 453 | -7.993  | 28.886 | 34.524 | 1.00 | 12.98 |
| ATOM | 1859 | N    | SER     | A | 454 | -6.301  | 28.786 | 36.002 | 1.00 | 10.78 |
| ATOM | 1860 | CA   | SER     | A | 454 | -5.584  | 29.858 | 35.390 | 1.00 | 9.42  |
| ATOM | 1861 | CB   | SER     | A | 454 | -4.341  | 30.410 | 36.146 | 1.00 | 8.01  |
| ATOM | 1862 | OG   | SER     | A | 454 | -4.692  | 30.709 | 37.471 | 1.00 | 8.77  |
| ATOM | 1863 | C    | SER     | A | 454 | -5.186  | 29.538 | 33.979 | 1.00 | 9.67  |
| ATOM | 1864 | O    | SER     | A | 454 | -5.237  | 30.413 | 33.113 | 1.00 | 9.80  |
| ATOM | 1865 | N    | LYS     | A | 455 | -4.691  | 28.304 | 33.763 | 1.00 | 11.07 |
| ATOM | 1866 | CA   | LYS     | A | 455 | -4.240  | 27.987 | 32.421 | 1.00 | 12.98 |
| ATOM | 1867 | CB   | LYS     | A | 455 | -3.599  | 26.587 | 32.376 | 1.00 | 13.14 |
| ATOM | 1868 | CG   | LYS     | A | 455 | -2.146  | 26.611 | 32.855 | 1.00 | 17.01 |
| ATOM | 1869 | CD   | LYS     | A | 455 | -1.656  | 25.166 | 32.882 | 1.00 | 19.15 |
| ATOM | 1870 | CE   | LYS     | A | 455 | -0.242  | 25.104 | 33.451 | 1.00 | 20.39 |
| ATOM | 1871 | NZ   | LYS     | A | 455 | 0.195   | 23.673 | 33.295 | 1.00 | 23.90 |
| ATOM | 1872 | C    | LYS     | A | 455 | -5.367  | 28.049 | 31.401 | 1.00 | 12.31 |
| ATOM | 1873 | O    | LYS     | A | 455 | -5.180  | 28.539 | 30.315 | 1.00 | 12.74 |
| ATOM | 1874 | N    | GLN     | A | 456 | -6.529  | 27.527 | 31.755 | 1.00 | 14.47 |
| ATOM | 1875 | NE2  | GLN     | A | 456 | -10.676 | 25.407 | 33.099 | 1.00 | 30.34 |
| ATOM | 1876 | OE1  | GLN     | A | 456 | -9.503  | 23.500 | 32.899 | 1.00 | 29.79 |
| ATOM | 1877 | CD   | GLN     | A | 456 | -9.664  | 24.686 | 32.606 | 1.00 | 28.31 |

|      | Atom | Type | Residue | ? | #   | X       | Y      | Z      | OCC  | B     |
|------|------|------|---------|---|-----|---------|--------|--------|------|-------|
| ATOM | 1878 | CG   | GLN     | A | 456 | -8.670  | 25.342 | 31.636 | 1.00 | 25.00 |
| ATOM | 1879 | CB   | GLN     | A | 456 | -8.814  | 26.832 | 31.511 | 1.00 | 19.95 |
| ATOM | 1880 | CA   | GLN     | A | 456 | -7.661  | 27.516 | 30.804 | 1.00 | 16.41 |
| ATOM | 1881 | C    | GLN     | A | 456 | -7.967  | 28.942 | 30.401 | 1.00 | 15.24 |
| ATOM | 1882 | O    | GLN     | A | 456 | -7.936  | 29.330 | 29.244 | 1.00 | 15.99 |
| ATOM | 1883 | N    | SER     | A | 457 | -8.038  | 29.821 | 31.393 | 1.00 | 14.14 |
| ATOM | 1884 | CA   | SER     | A | 457 | -8.377  | 31.231 | 31.194 | 1.00 | 14.81 |
| ATOM | 1885 | CB   | SER     | A | 457 | -8.518  | 31.976 | 32.530 | 1.00 | 15.12 |
| ATOM | 1886 | OG   | SER     | A | 457 | -9.565  | 31.464 | 33.315 | 1.00 | 16.45 |
| ATOM | 1887 | C    | SER     | A | 457 | -7.354  | 31.967 | 30.377 | 1.00 | 12.94 |
| ATOM | 1888 | O    | SER     | A | 457 | -7.697  | 32.696 | 29.467 | 1.00 | 12.19 |
| ATOM | 1889 | N    | ILE     | A | 458 | -6.051  | 31.825 | 30.722 | 1.00 | 12.21 |
| ATOM | 1890 | CA   | ILE     | A | 458 | -5.038  | 32.567 | 29.982 | 1.00 | 9.86  |
| ATOM | 1891 | CB   | ILE     | A | 458 | -3.699  | 32.500 | 30.795 | 1.00 | 11.36 |
| ATOM | 1892 | CG2  | ILE     | A | 458 | -2.555  | 32.898 | 29.890 | 1.00 | 6.36  |
| ATOM | 1893 | CG1  | ILE     | A | 458 | -3.853  | 33.384 | 32.036 | 1.00 | 9.88  |
| ATOM | 1894 | CD1  | ILE     | A | 458 | -2.730  | 33.281 | 33.059 | 1.00 | 11.89 |
| ATOM | 1895 | C    | ILE     | A | 458 | -4.854  | 32.048 | 28.573 | 1.00 | 9.53  |
| ATOM | 1896 | O    | ILE     | A | 458 | -4.640  | 32.816 | 27.634 | 1.00 | 9.61  |
| ATOM | 1897 | N    | TYR     | A | 459 | -4.939  | 30.731 | 28.423 | 1.00 | 9.48  |
| ATOM | 1898 | CA   | TYR     | A | 459 | -4.767  | 30.100 | 27.112 | 1.00 | 11.60 |
| ATOM | 1899 | CB   | TYR     | A | 459 | -5.038  | 28.600 | 27.250 | 1.00 | 11.22 |
| ATOM | 1900 | CG   | TYR     | A | 459 | -5.045  | 27.843 | 25.943 | 1.00 | 16.31 |
| ATOM | 1901 | CD1  | TYR     | A | 459 | -4.013  | 27.976 | 25.041 | 1.00 | 16.99 |
| ATOM | 1902 | CE1  | TYR     | A | 459 | -4.028  | 27.303 | 23.827 | 1.00 | 19.40 |
| ATOM | 1903 | CD2  | TYR     | A | 459 | -6.103  | 26.999 | 25.626 | 1.00 | 18.93 |
| ATOM | 1904 | CE2  | TYR     | A | 459 | -6.108  | 26.299 | 24.422 | 1.00 | 21.51 |
| ATOM | 1905 | CZ   | TYR     | A | 459 | -5.075  | 26.458 | 23.532 | 1.00 | 20.71 |
| ATOM | 1906 | OH   | TYR     | A | 459 | -5.095  | 25.772 | 22.341 | 1.00 | 21.74 |
| ATOM | 1907 | C    | TYR     | A | 459 | -5.720  | 30.750 | 26.110 | 1.00 | 12.72 |
| ATOM | 1908 | O    | TYR     | A | 459 | -5.334  | 31.252 | 25.073 | 1.00 | 14.82 |
| ATOM | 1909 | N    | LYS     | A | 460 | -6.974  | 30.779 | 26.528 | 1.00 | 14.14 |
| ATOM | 1910 | NZ   | LYS     | A | 460 | -10.468 | 26.961 | 25.743 | 1.00 | 30.41 |
| ATOM | 1911 | CE   | LYS     | A | 460 | -9.733  | 27.718 | 24.702 | 1.00 | 27.82 |
| ATOM | 1912 | CD   | LYS     | A | 460 | -9.809  | 29.219 | 24.921 | 1.00 | 26.35 |
| ATOM | 1913 | CG   | LYS     | A | 460 | -9.794  | 29.689 | 26.345 | 1.00 | 23.26 |
| ATOM | 1914 | CB   | LYS     | A | 460 | -9.375  | 31.156 | 26.477 | 1.00 | 19.80 |
| ATOM | 1915 | CA   | LYS     | A | 460 | -8.043  | 31.371 | 25.721 | 1.00 | 18.07 |
| ATOM | 1916 | C    | LYS     | A | 460 | -7.739  | 32.806 | 25.384 | 1.00 | 16.65 |
| ATOM | 1917 | O    | LYS     | A | 460 | -7.735  | 33.206 | 24.228 | 1.00 | 16.84 |
| ATOM | 1918 | N    | THR     | A | 461 | -7.225  | 33.546 | 26.348 | 1.00 | 14.44 |
| ATOM | 1919 | CA   | THR     | A | 461 | -6.847  | 34.932 | 26.129 | 1.00 | 14.79 |
| ATOM | 1920 | CB   | THR     | A | 461 | -6.597  | 35.590 | 27.509 | 1.00 | 13.79 |
| ATOM | 1921 | OG1  | THR     | A | 461 | -7.813  | 35.528 | 28.254 | 1.00 | 13.87 |
| ATOM | 1922 | CG2  | THR     | A | 461 | -6.192  | 37.054 | 27.345 | 1.00 | 16.01 |
| ATOM | 1923 | C    | THR     | A | 461 | -5.709  | 35.061 | 25.159 | 1.00 | 14.88 |
| ATOM | 1924 | O    | THR     | A | 461 | -5.830  | 35.765 | 24.142 | 1.00 | 14.86 |
| ATOM | 1925 | N    | ILE     | A | 462 | -4.569  | 34.417 | 25.419 | 1.00 | 14.52 |
| ATOM | 1926 | CA   | ILE     | A | 462 | -3.422  | 34.528 | 24.542 | 1.00 | 17.34 |
| ATOM | 1927 | CB   | ILE     | A | 462 | -2.223  | 33.642 | 24.975 | 1.00 | 18.43 |
| ATOM | 1928 | CG2  | ILE     | A | 462 | -1.130  | 33.699 | 23.904 | 1.00 | 20.28 |
| ATOM | 1929 | CG1  | ILE     | A | 462 | -1.643  | 34.018 | 26.316 | 1.00 | 18.70 |
| ATOM | 1930 | CD1  | ILE     | A | 462 | -0.726  | 32.967 | 26.946 | 1.00 | 19.10 |
| ATOM | 1931 | C    | ILE     | A | 462 | -3.757  | 34.102 | 23.124 | 1.00 | 18.59 |



|      | Atom | Type | Residue | ? | #   | X      | Y      | Z      | OCC  | B     |
|------|------|------|---------|---|-----|--------|--------|--------|------|-------|
| ATOM | 1932 | O    | ILE     | A | 462 | -3.420 | 34.813 | 22.189 | 1.00 | 17.11 |
| ATOM | 1933 | N    | GLU     | A | 463 | -4.473 | 32.979 | 22.968 | 1.00 | 22.82 |
| ATOM | 1934 | OE2  | GLU     | A | 463 | -8.026 | 29.422 | 22.532 | 1.00 | 41.03 |
| ATOM | 1935 | OE1  | GLU     | A | 463 | -7.006 | 28.787 | 20.674 | 1.00 | 39.73 |
| ATOM | 1936 | CD   | GLU     | A | 463 | -7.293 | 29.635 | 21.536 | 1.00 | 39.22 |
| ATOM | 1937 | CG   | GLU     | A | 463 | -6.723 | 31.032 | 21.405 | 1.00 | 36.15 |
| ATOM | 1938 | CB   | GLU     | A | 463 | -5.228 | 31.095 | 21.624 | 1.00 | 30.56 |
| ATOM | 1939 | CA   | GLU     | A | 463 | -4.692 | 32.520 | 21.587 | 1.00 | 26.30 |
| ATOM | 1940 | C    | GLU     | A | 463 | -5.492 | 33.530 | 20.800 | 1.00 | 27.72 |
| ATOM | 1941 | O    | GLU     | A | 463 | -5.233 | 33.704 | 19.607 | 1.00 | 29.03 |
| ATOM | 1942 | N    | SER     | A | 464 | -6.399 | 34.283 | 21.418 | 1.00 | 26.79 |
| ATOM | 1943 | CA   | SER     | A | 464 | -7.190 | 35.312 | 20.764 | 1.00 | 26.80 |
| ATOM | 1944 | CB   | SER     | A | 464 | -8.395 | 35.611 | 21.666 | 1.00 | 25.15 |
| ATOM | 1945 | OG   | SER     | A | 464 | -9.060 | 36.806 | 21.404 | 1.00 | 25.60 |
| ATOM | 1946 | C    | SER     | A | 464 | -6.434 | 36.623 | 20.582 | 1.00 | 27.79 |
| ATOM | 1947 | O    | SER     | A | 464 | -6.686 | 37.340 | 19.612 | 1.00 | 27.52 |
| ATOM | 1948 | N    | LYS     | A | 465 | -5.598 | 36.959 | 21.560 | 1.00 | 25.83 |
| ATOM | 1949 | CA   | LYS     | A | 465 | -4.956 | 38.267 | 21.585 | 1.00 | 28.04 |
| ATOM | 1950 | CB   | LYS     | A | 465 | -5.065 | 38.846 | 22.993 | 1.00 | 28.65 |
| ATOM | 1951 | CG   | LYS     | A | 465 | -6.217 | 39.766 | 23.316 | 1.00 | 30.43 |
| ATOM | 1952 | CD   | LYS     | A | 465 | -7.570 | 39.136 | 23.099 | 1.00 | 31.72 |
| ATOM | 1953 | CE   | LYS     | A | 465 | -8.699 | 40.165 | 23.068 | 1.00 | 32.17 |
| ATOM | 1954 | NZ   | LYS     | A | 465 | -8.593 | 41.165 | 24.149 | 1.00 | 32.20 |
| ATOM | 1955 | C    | LYS     | A | 465 | -3.505 | 38.293 | 21.145 | 1.00 | 27.28 |
| ATOM | 1956 | O    | LYS     | A | 465 | -3.053 | 39.353 | 20.704 | 1.00 | 27.45 |
| ATOM | 1957 | N    | ALA     | A | 466 | -2.767 | 37.193 | 21.184 | 1.00 | 28.49 |
| ATOM | 1958 | CA   | ALA     | A | 466 | -1.373 | 37.191 | 20.753 | 1.00 | 28.95 |
| ATOM | 1959 | CB   | ALA     | A | 466 | -0.788 | 35.788 | 20.750 | 1.00 | 27.44 |
| ATOM | 1960 | C    | ALA     | A | 466 | -1.152 | 37.821 | 19.385 | 1.00 | 30.12 |
| ATOM | 1961 | O    | ALA     | A | 466 | -0.295 | 38.708 | 19.256 | 1.00 | 28.37 |
| ATOM | 1962 | N    | GLN     | A | 467 | -1.922 | 37.440 | 18.373 | 1.00 | 30.63 |
| ATOM | 1963 | NE2  | GLN     | A | 467 | 0.360  | 36.582 | 14.061 | 1.00 | 41.77 |
| ATOM | 1964 | OE1  | GLN     | A | 467 | -0.196 | 35.394 | 15.846 | 1.00 | 42.22 |
| ATOM | 1965 | CD   | GLN     | A | 467 | -0.524 | 36.191 | 14.967 | 1.00 | 40.84 |
| ATOM | 1966 | CG   | GLN     | A | 467 | -1.903 | 36.768 | 14.813 | 1.00 | 40.14 |
| ATOM | 1967 | CB   | GLN     | A | 467 | -2.609 | 37.306 | 16.027 | 1.00 | 36.55 |
| ATOM | 1968 | CA   | GLN     | A | 467 | -1.712 | 38.007 | 17.038 | 1.00 | 33.94 |
| ATOM | 1969 | C    | GLN     | A | 467 | -1.891 | 39.519 | 16.996 | 1.00 | 33.19 |
| ATOM | 1970 | O    | GLN     | A | 467 | -1.208 | 40.231 | 16.271 | 1.00 | 33.32 |
| ATOM | 1971 | N    | GLU     | A | 468 | -2.797 | 40.063 | 17.768 | 1.00 | 33.44 |
| ATOM | 1972 | OE2  | GLU     | A | 468 | -7.657 | 40.802 | 18.969 | 1.00 | 44.61 |
| ATOM | 1973 | OE1  | GLU     | A | 468 | -6.465 | 41.900 | 20.497 | 1.00 | 44.24 |
| ATOM | 1974 | CD   | GLU     | A | 468 | -6.664 | 41.480 | 19.332 | 1.00 | 44.10 |
| ATOM | 1975 | CG   | GLU     | A | 468 | -5.602 | 41.832 | 18.305 | 1.00 | 41.64 |
| ATOM | 1976 | CB   | GLU     | A | 468 | -4.238 | 41.582 | 18.934 | 1.00 | 38.28 |
| ATOM | 1977 | CA   | GLU     | A | 468 | -3.092 | 41.457 | 17.917 | 1.00 | 35.15 |
| ATOM | 1978 | C    | GLU     | A | 468 | -1.956 | 42.299 | 18.485 | 1.00 | 33.88 |
| ATOM | 1979 | O    | GLU     | A | 468 | -1.706 | 43.397 | 17.980 | 1.00 | 32.88 |
| ATOM | 1980 | N    | CYS     | A | 469 | -1.382 | 41.873 | 19.618 | 1.00 | 32.54 |
| ATOM | 1981 | CA   | CYS     | A | 469 | -0.374 | 42.738 | 20.230 | 1.00 | 32.43 |
| ATOM | 1982 | CB   | CYS     | A | 469 | -1.019 | 43.591 | 21.320 | 1.00 | 34.38 |
| ATOM | 1983 | SG   | CYS     | A | 469 | -1.294 | 42.874 | 22.918 | 1.00 | 36.46 |
| ATOM | 1984 | C    | CYS     | A | 469 | 0.888  | 42.055 | 20.713 | 1.00 | 29.85 |
| ATOM | 1985 | O    | CYS     | A | 469 | 1.786  | 42.811 | 21.105 | 1.00 | 30.62 |

|      | Atom |         |   |     |        |        |        |      |       |  |
|------|------|---------|---|-----|--------|--------|--------|------|-------|--|
|      | Type | Residue | Z | #   | X      | Y      | Z      | OCC  | B     |  |
| ATOM | 1986 | N PHE   | A | 470 | 1.027  | 40.739 | 20.624 | 1.00 | 26.22 |  |
| ATOM | 1987 | CA PHE  | A | 470 | 2.314  | 40.147 | 21.073 | 1.00 | 25.07 |  |
| ATOM | 1988 | CB PHE  | A | 470 | 2.163  | 38.694 | 21.471 | 1.00 | 21.88 |  |
| ATOM | 1989 | CG PHE  | A | 470 | 1.492  | 38.480 | 22.808 | 1.00 | 21.60 |  |
| ATOM | 1990 | CD1 PHE | A | 470 | 0.810  | 39.497 | 23.450 | 1.00 | 19.78 |  |
| ATOM | 1991 | CD2 PHE | A | 470 | 1.556  | 37.251 | 23.414 | 1.00 | 19.41 |  |
| ATOM | 1992 | CE1 PHE | A | 470 | 0.182  | 39.309 | 24.658 | 1.00 | 20.26 |  |
| ATOM | 1993 | CE2 PHE | A | 470 | 0.932  | 37.046 | 24.634 | 1.00 | 20.13 |  |
| ATOM | 1994 | CZ PHE  | A | 470 | 0.257  | 38.065 | 25.257 | 1.00 | 20.62 |  |
| ATOM | 1995 | C PHE   | A | 470 | 3.351  | 40.383 | 19.999 | 1.00 | 24.85 |  |
| ATOM | 1996 | O PHE   | A | 470 | 2.994  | 40.592 | 18.836 | 1.00 | 23.37 |  |
| ATOM | 1997 | N GLN   | A | 471 | 4.610  | 40.404 | 20.389 | 1.00 | 23.76 |  |
| ATOM | 1998 | CA GLN  | A | 471 | 5.714  | 40.672 | 19.491 | 1.00 | 25.96 |  |
| ATOM | 1999 | CB GLN  | A | 471 | 6.350  | 42.028 | 19.794 | 1.00 | 27.26 |  |
| ATOM | 2000 | CG GLN  | A | 471 | 5.453  | 43.201 | 19.442 | 1.00 | 31.81 |  |
| ATOM | 2001 | CD GLN  | A | 471 | 6.014  | 44.575 | 19.678 | 1.00 | 33.37 |  |
| ATOM | 2002 | OE1 GLN | A | 471 | 5.258  | 45.547 | 19.668 | 1.00 | 35.13 |  |
| ATOM | 2003 | NE2 GLN | A | 471 | 7.323  | 44.723 | 19.885 | 1.00 | 35.41 |  |
| ATOM | 2004 | C GLN   | A | 471 | 6.772  | 39.578 | 19.615 | 1.00 | 25.85 |  |
| ATOM | 2005 | O GLN   | A | 471 | 6.668  | 38.670 | 20.433 | 1.00 | 23.32 |  |
| ATOM | 2006 | N GLU   | A | 472 | 7.771  | 39.683 | 18.760 | 1.00 | 27.21 |  |
| ATOM | 2007 | OE2 GLU | A | 472 | 8.898  | 41.817 | 17.307 | 1.00 | 43.27 |  |
| ATOM | 2008 | OE1 GLU | A | 472 | 9.685  | 41.624 | 15.282 | 1.00 | 44.72 |  |
| ATOM | 2009 | CD GLU  | A | 472 | 9.267  | 41.115 | 16.344 | 1.00 | 42.17 |  |
| ATOM | 2010 | CG GLU  | A | 472 | 9.207  | 39.605 | 16.387 | 1.00 | 39.41 |  |
| ATOM | 2011 | CB GLU  | A | 472 | 9.836  | 38.975 | 17.600 | 1.00 | 34.14 |  |
| ATOM | 2012 | CA GLU  | A | 472 | 8.867  | 38.730 | 18.759 | 1.00 | 30.87 |  |
| ATOM | 2013 | C GLU   | A | 472 | 9.656  | 38.993 | 20.037 | 1.00 | 30.26 |  |
| ATOM | 2014 | O GLU   | A | 472 | 9.773  | 40.161 | 20.396 | 1.00 | 29.23 |  |
| ATOM | 2015 | N ARG   | A | 473 | 10.256 | 37.970 | 20.584 | 1.00 | 31.97 |  |
| ATOM | 2016 | CA ARG  | A | 473 | 11.073 | 38.106 | 21.778 | 1.00 | 34.21 |  |
| ATOM | 2017 | CB ARG  | A | 473 | 11.230 | 36.691 | 22.340 | 1.00 | 34.97 |  |
| ATOM | 2018 | CG ARG  | A | 473 | 12.230 | 36.454 | 23.443 | 1.00 | 37.52 |  |
| ATOM | 2019 | CD ARG  | A | 473 | 11.661 | 35.449 | 24.436 | 1.00 | 39.68 |  |
| ATOM | 2020 | NE ARG  | A | 473 | 12.564 | 35.155 | 25.532 | 1.00 | 41.06 |  |
| ATOM | 2021 | CZ ARG  | A | 473 | 12.469 | 35.726 | 26.729 | 1.00 | 42.18 |  |
| ATOM | 2022 | NH1 ARG | A | 473 | 13.327 | 35.423 | 27.693 | 1.00 | 42.83 |  |
| ATOM | 2023 | NH2 ARG | A | 473 | 11.559 | 36.660 | 26.960 | 1.00 | 42.33 |  |
| ATOM | 2024 | C ARG   | A | 473 | 12.451 | 38.665 | 21.456 | 1.00 | 36.39 |  |
| ATOM | 2025 | O ARG   | A | 473 | 13.092 | 38.294 | 20.489 | 1.00 | 36.44 |  |
| ATOM | 2026 | N SER   | A | 474 | 12.918 | 39.567 | 22.276 | 1.00 | 37.92 |  |
| ATOM | 2027 | OG SER  | A | 474 | 15.308 | 38.413 | 23.524 | 1.00 | 36.38 |  |
| ATOM | 2028 | CB SER  | A | 474 | 15.293 | 39.122 | 22.290 | 1.00 | 37.61 |  |
| ATOM | 2029 | CA SER  | A | 474 | 14.200 | 40.202 | 22.359 | 1.00 | 37.96 |  |
| ATOM | 2030 | C SER   | A | 474 | 14.436 | 41.341 | 21.403 | 1.00 | 39.67 |  |
| ATOM | 2031 | O SER   | A | 474 | 13.589 | 42.259 | 21.336 | 1.00 | 40.16 |  |
| END  |      |         |   |     |        |        |        |      |       |  |

#### Example 5 - TACE Inhibitor Design

The TACE x-ray diffraction coordinates were read into a Sybyl v.6.3 (Tripos Associates) software package and the x-ray structure analyzed graphically. The regions within the original x-ray coordinates were corrected for chirality and atom type. The modified x-ray model of TACE was energy minimized until all the TACE structural parameters were at their equilibrium or optimal values. The energy minimized structure was then compared to the original structure to confirm the absence of anomalies.

Sites of specific interaction(s) between TACE and the co-crystallized inhibitor were identified. The inhibitor was then removed from the X-ray complex model, leaving only the TACE structural model.

Candidate inhibitors were chosen based upon the sites of interaction with TACE and the candidate inhibitor in light of the sites of interaction identified previously for the co-crystallized inhibitor. Once specific candidate inhibitor-TACE interactions were determined, docking studies were performed to provide preliminary “modeled” complexes of selected candidate inhibitors with TACE.

Constrained conformational analysis was performed using molecular dynamics (MD) to check the integrity of the modeled TACE-inhibitor complex. Once the complex reached its most favorable conformational state, the structure as proposed by the MD study was analyzed visually to insure that the modeled complex complied with known experimental SAR/QSAR based on measured binding affinities.

The modeled candidate inhibitor-TACE complex was analyzed. The region of the complex associated with the S1' regions of TACE containing a small solvent exposed channel was chosen as a target region for modification. A single modification, a benzyl group which becomes embedded within the target region, was selected based upon computational and synthetic chemical principles. The benzyl group was oriented on an appropriate zinc chelator core so as to be projected into the S1' S3' pocket. This modification converts an inhibitor which was generally MMP

selective to one which is TACE selective. IC<sub>50</sub> data for the inhibitor with a benzyl modification confirm this selectivity.

Structure-based analoging for optimization of inhibitor potency, selectivity and physical drug-like properties was performed in an iterative manner.

#### Example 6 - Measuring TACE Inhibition

250μM peptide substrate (Ac-SPLAQAVRSSSR-NH<sub>2</sub>) (SEQ ID NO: 9) was incubated with 3.7 U/μL TACE in a buffer containing 10mM TRIS HCl, pH 7.4, 10% glycerol at 25 degrees C. The reaction was quenched with 1% TFA (final concentration) after two hours. The reaction mixture was separated by HPLC on a Hewlett-Packard 1150. The product formation was monitored by absorbance at 220nm.

The linearity of the reaction was confirmed ( $r^2 > 0.85$ ). The mean ( $x \pm \text{sem}$ ) of the control rate was calculated and compared for statistical significance ( $p < 0.05$ ) with drug-tested rates using Dunnett's multiple comparison test. Dose-response relationships were generated using multiple doses of drug and IC<sub>50</sub> values with 95% CI were estimated using linear regression.

From the foregoing description and examples, one skilled in the art can ascertain the essential characteristics of the invention and, without departing from the spirit and scope of the invention, can make changes, modifications, and variations of the invention to adapt it to various uses and conditions. Additionally, the disclosure of all publications and patent applications cited above, including U.S. provisional patent application serial No. 60/073,709 and U.S. provisional patent application serial No. 60/135,499, are expressly incorporated herein by reference in their entireties to the same extent as if each were incorporated by reference individually.